# **WEST Search History**

Hide Items Restore Clear Cancel

DATE: Friday, July 22, 2005

| Hide? | Set Name | Query  | Hit Count |
|-------|----------|--|-----------|
|       | DB = USI | PT; PLUR=YES; OP=OR                                    |           |
|       | L8       | capping same membrane same \$saccharid\$               | 19        |
|       | L7       | capping same (\$antibod? or adhes?) same \$saccharid\$ | 4         |
|       | L6       | capping same (\$antibod? or adhes?) same membrane      | 20        |
|       | L5       | cap? same (antibod? or adhes?) same membran?           | 58        |
|       | DB=PG    | PB,USPT; PLUR=YES; OP=OR                               |           |
|       | L4       | cap? same (antibod? or adhes?) same membran?           | 107       |
|       | L3       | 2004013720.pn.   | 0         |
|       | L2       | differ\$ with head with epitope                        | 10        |
|       | L1       | bilayer same ((conjugate or conjugated) WITH head)     | 17        |

**END OF SEARCH HISTORY** 

# **WEST Search History**

Hide Items Restore Clear Cancel

DATE: Friday, July 22, 2005

**END OF SEARCH HISTORY** 

| Hide? | Hide? Set Name Query |  |    |  |  |
|-------|----------------------|--|----|--|--|
|       | DB=PG                | PB,USPT; PLUR=YES; OP=OR                           |    |  |  |
|       | L2                   | differ\$ with head with epitope                    | 10 |  |  |
|       | L1                   | bilayer same ((conjugate or conjugated) WITH head) | 17 |  |  |

120 27,32 44 48/56 44 47/40 50 6151 1-4-01 1,9,10,11,13 60/245,140 18,19,25

77,28,27,30,31,36

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FILE 'HOME' ENTERED AT 15:58:16 ON 22 JUL 2005

=> fil medline biosis caplus embase wpids COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

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FILE 'WPIDS' ENTERED AT 15:58:37 ON 22 JUL 2005 COPYRIGHT (C) 2005 THE THOMSON CORPORATION

- => head (s) different (s) epitope L1 10 HEAD (S) DIFFERENT (S) EPITOPE
- => head (s) differ? (s) epitope L2 16 HEAD (S) DIFFER? (S) EPITOPE
- => t ti 13 1-12
- L3 ANSWER 1 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
  TI New bispecific antibodies that bind two different targets, useful for diagnosing, preventing or treating diseases such as a hyperproliferative (e.g. cancer), cardiovascular, neurodegenerative, metabolic or an autoimmune disease.
- L3 ANSWER 2 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Detecting a cancer cell in a subject sample, also related to cancer treatments, comprises determining the level of nucleic acid that is linked to map position 8q22.3 of the human genome or its expression product.
- L3 ANSWER 3 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New purified thrombospondin fragment extracted from a body fluid, useful for diagnosing cancer e.g. adenoma, adenocarcinoma, carcinoma, lymphoma or leukemia or as calibrators, indicators, immunogens and analytes.

- L3 ANSWER 4 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Selecting an antibody from a phage display library using sequential antigen panning, useful for treating or reducing infections, such as bacterial, virus and parasitic infection, and for inhibiting cancers.
- L3 ANSWER 5 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- Diagnosing and/or treating cancer, such as brain, lymphatic, liver, stomach, testicular, cervical, endometrial, renal, lung and ovarian cancers, leukemia and melanoma, comprises using soluble MIC polypeptides as markers.
- L3 ANSWER 6 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Preventing, treating or managing cancer in a patient comprises administering to the patient VITAXIN or an antibody or its fragment that competes with VITAXIN for binding to Integrin alphavbeta3 and one or more other cancer therapies.
- L3 ANSWER 7 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Nanoparticle useful as synthetic vaccine, comprises carrier, and ligands displayed on the carrier, where ligands form polyvalent binding unit to produce interaction between nanoparticle and receptors on target.
- L3 ANSWER 8 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New Major Histocompatibility Complex (MHC) molecule construct, useful for treating, preventing, stabilizing or alleviating a disease involving MHC recognizing cells e.g., cancer.
- L3 ANSWER 9 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Epitopes formed by non-covalent association of conjugates, useful in therapeutic, prophylactic or diagnostic methods.
- L3 ANSWER 10 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Inducing human immunodeficiency virus-specific helper T-cell responses.
- L3 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 1
- TI Plakophilin, armadillo repeats, and nuclear localization.
- L3 ANSWER 12 OF 12 MEDLINE on STN DUPLICATE 2
- TI Differential localization of two epitopes of Escherichia coli ribosomal protein L2 on the large ribosomal subunit by immune electron microscopy using monoclonal antibodies.

#### => d ibib abs 13 9

L3 ANSWER 9 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-102938 [11] WPIDS

DOC. NO. NON-CPI: N2001-076388 DOC. NO. CPI: C2001-030197

TITLE: Epitopes formed by non-covalent association of

conjugates, useful in therapeutic, prophylactic or

diagnostic methods.

DERWENT CLASS: B04 S03

INVENTOR(S): NEW, R; TOTH, I

PATENT ASSIGNEE(S): (PROX-N) PROXIMA CONCEPTS LTD; (MOZA-N) MOZAICO DISCOVERY

LTD; (MOZA-N) MOZAIC DISCOVERY LTD; (PROV-N) PROVALIS UK

LTD

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

```
A1 20010104 (200111) * EN
WO 2001001140
                                          39
   RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW M2
      NL OA PT SD SE SL SZ TZ UG ZW
    W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
      EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
      LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
      SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000056923 A 20010131 (200124)
               A 20020312 (200226)
BR 2000012002
               A1 20020327 (200229) EN
EP 1190255
    R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
      RO SE SI
CN 1359469
              A 20020717 (200268)
KR 2002042537
             A 20020605 (200277)
JP 2003503424 W 20030128 (200309)
                                          29
              B2 20040729 (200472)
AU 775310
```

#### APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
| WO 2001001140 | A1   | WO 2000-GB2465 | 20000627 |
| AU 2000056923 | Α    | AU 2000-56923  | 20000627 |
| BR 2000012002 | Α    | BR 2000-12002  | 20000627 |
|               |      | WO 2000-GB2465 | 20000627 |
| EP 1190255    | A1   | EP 2000-942216 | 20000627 |
|               |      | WO 2000-GB2465 | 20000627 |
| CN 1359469    | Α    | CN 2000-809653 | 20000627 |
| KR 2002042537 | Α    | KR 2001-716715 | 20011227 |
| JP 2003503424 | W    | WO 2000-GB2465 | 20000627 |
|               |      | JP 2001-507094 | 20000627 |
| AU 775310     | B2   | AU 2000-56923  | 20000627 |

#### FILING DETAILS:

| PATENT NO     | KIND              | PATENT NO     |  |
|---------------|-------------------|---------------|--|
| AU 2000056923 | A Based on        | WO 2001001140 |  |
| BR 2000012002 | A Based on        | WO 2001001140 |  |
| EP 1190255    | Al Based on       | WO 2001001140 |  |
| JP 2003503424 | W Based on        | WO 2001001140 |  |
| AU 775310     | B2 Previous Publ. | AU 2000056923 |  |
|               | Based on          | WO 2001001140 |  |

PRIORITY APPLN. INFO: GB 1999-15074 19990628

AN 2001-102938 [11] WPIDS

AB WO 200101140 A UPAB: 20010224

NOVELTY - Epitopes are formed by non-covalent association of conjugates, and assemblies composed of combinations of different head groups can elicit biological responses or participate in binding with biological receptors that assemblies of single head groups cannot.

DETAILED DESCRIPTION - A composition for interacting with a ligand comprises a non-covalent association of **different** conjugates, each conjugate comprising a **head** group and a tail group, where the tail groups form a hydrophobic aggregation and the conjugates are movable within the association so that, in the presence of a ligand, at least 2 of the **head** groups are appropriately positioned to form an **epitope** capable of interacting with the ligand more strongly than each of the **head** groups individually. An INDEPENDENT CLAIM is included for the following:

- (a) preparation of the composition; and
- (b) a method for producing a molecule for interacting with a ligand,

comprising producing a composition as above; identifying the head groups which form an epitope for the ligand; and producing a molecule incorporating the functional groups of the head groups, optionally spaced apart by 1 or more linker groups so that the molecule is capable of interacting with the ligand more strongly than each of the head groups individually.

 $\mbox{USE}$  -  $\mbox{\sc The}$  compositions are useful in the rapeutic, prophylactic or diagnostic methods.

ADVANTAGE - Strong specific binding interactions can be achieved with conjugates in which the head groups are small compared to conventional biological receptors, e.g. if the head group is an oligo-peptide, then the length of the peptide chain would be at most 10 (preferably at most 6) amino acids, and compositions can be made less immunogenic than their protein counterparts.

Dwg.0/2

=> d ibib abs 13 1-8, 10-12

L3 ANSWER 1 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-091969 [10] WPIDS

DOC. NO. CPI: C2005-031094

TITLE: New bispecific antibodies that bind two different

targets, useful for diagnosing, preventing or treating diseases such as a hyperproliferative (e.g. cancer), cardiovascular, neurodegenerative, metabolic or an

autoimmune disease.

DERWENT CLASS: B04 D16

INVENTOR(S): HANSEN, H J; MCBRIDE, W J; QU, Z

PATENT ASSIGNEE(S): (IMMU-N) IMMUNOMEDICS INC

COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2005004809 A2 20050120 (200510) \* EN 163

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE

LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ

OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG

US UZ VC VN YU ZA ZM ZW

US 2005100543 A1 20050512 (200532)

# APPLICATION DETAILS:

| PATENT NO                      | KIND                 | APPLICATION                                    | DATE                             |
|--------------------------------|----------------------|--|----------------------------------|
| WO 2005004809<br>US 2005100543 | A2<br>A1 Provisional | WO 2004-US20995 US 2003-483832P US 2004-882151 | 20040701<br>20030701<br>20040701 |

PRIORITY APPLN. INFO: US 2003-483832P 20030701; US

2004-882151 20040701

AN 2005-091969 [10] WPIDS

AB WO2005004809 A UPAB: 20050211

NOVELTY - A bispecific antibody comprising the structure (IgG1)-(scFv)2, is new. The antibody comprises a pair of heavy chains and a pair of light chains, where each heavy chain comprises an IgG1 heavy chain and an scFv, where the scFv is fused to the C-terminus of the IgG1 heavy chain,

optionally via a linker peptide.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) a binding complex comprising a tetravalent binding molecule bound to a targetable construct, where the tetravalent binding molecule comprises 2 binding sites for a carrier epitope and 2 binding sites for a target epitope, and where the targetable construct comprises a molecular scaffold and at least 2 carrier epitopes;
  - (2) treating a disease in a subject;
  - (3) diagnosing/detecting a disease in a subject;
- (4) a kit comprising a tetravalent binding molecule comprising 2 binding sites for a carrier epitope and 2 binding sites for a target epitope; optionally, a clearing agent; and a targetable construct comprising a molecular scaffold and at least 2 carrier epitopes; and
- (5) a pharmaceutical composition comprising the bispecific antibody cited above.

ACTIVITY - Cytostatic; Cardiovascular-Gen.; Neuroprotective; Endocrine-Gen.; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The composition and methods are useful for diagnosing, preventing or treating diseases such as a hyperproliferative disease, pathogenic disease, cancer, cardiovascular disease, neurodegenerative disease, metabolic disease, or autoimmune disease.

Dwg.0/8

L3 ANSWER 2 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-248472 [23] WPIDS

CROSS REFERENCE: 2004-315574 [29]
DOC. NO. NON-CPI: N2004-197115
DOC. NO. CPI: C2004-097127

TITLE: Detecting a cancer cell in a subject sample, also related

to cancer treatments, comprises determining the level of nucleic acid that is linked to map position 8q22.3 of the

human genome or its expression product.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): CLANCY, J; HENDERSON, M; HENSHALL, S; O'BRIEN, P;

SAUNDERS, D; SUTHERLAND, R; WATTS, C; OBRIEN, P

PATENT ASSIGNEE(S): (GARV-N) GARVAN INST MEDICAL RES

COUNTRY COUNT: 106

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------|------|------|------|----|----|
|           |      |      |      |    |    |

WO 2004022750 A1 20040318 (200423) \* EN 331

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH

PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC

VN YU ZA ZM ZW

AU 2003257275 A1 20040329 (200459) EP 1539957 A1 20050615 (200539) EN

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

# APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
| WO 2004022750 | A1   | WO 2003-AU1164 | 20030905 |
| AU 2003257275 | A1   | AU 2003-257275 | 20030905 |

EP 1539957 A1 EP 2003-793494 20030905 WO 2003-AU1164 20030905

# FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2003257275 | Al Based on | WO 2004022750 |
| EP 1539957    | Al Based on | WO 2004022750 |

PRIORITY APPLN. INFO: US 2002-425218P 20021107; AU 2002-951346 20020905

AN 2004-248472 [23] WPIDS

CR 2004-315574 [29]

AB W02004022750 A UPAB: 20050621

NOVELTY - Detecting a cancer cell in a subject comprises determining the level of nucleic acid (Edd) that is linked to map position 8q22.3 of the human genome or its expression product in a sample of the subject, where an elevated level of the nucleic acid or polypeptide is indicative of cancer in the subject.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) a method for diagnosing a cancer or predicting recurrence of a cancer in a subject comprising determining the level of mRNA or protein encoded by nucleic acid as cited above;
  - (2) the isolated nucleic acid molecule for detecting cancer cell;
  - (3) an isolated or recombinant protein complex;
  - (4) an antibody that binds to the protein complex;
- (5) a kit for detecting or producing a protein complex, comprising an EDD polypeptide or a portion of an EDD polypeptide and a second polypeptides selected from a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein or its portion, where the portion of the second polypeptide is sufficient to bind to the EDD polypeptide or the portion of an EDD polypeptide;
  - (6) methods for isolating the protein complex;
- (7) a method for determining a predisposition for disease, or disease state:
- (8) a method for determining a modulator of the activity, formation or stability of an isolated or recombinant protein complex;
- (9) a method for determining a modulator of the level of protein complex formation;
- (10) a method for treating a condition associated with elevated expression of EDD protein in a cell;
- (11) an antisense nucleic acid, ribozyme, PNA, interfering RNA or siRNA; and
- (12) a pharmaceutical composition comprising the antisense nucleic acid, ribozyme, PNA, interfering RNA or siRNA.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The methods and modulator are useful for treating a condition associated with EDD over expression such as cancer, e.g. squamous cell carcinoma, hepatocellular carcinoma, ovarian cancer, breast cancer, melanoma, head and neck cancer, adenocarcinoma, squamous lung cancer, gastrointestinal cancer (e.g. gastric, colon, or pancreatic cancer), renal cell cancer, bladder cancer, prostate cancer, non-squamous carcinoma, glioblastoma and medulloblastoma. The components and composition are useful for reducing the expression of EDD in a cell to inhibit cellular proliferation (all claimed).

Dwg.0/29

L3 ANSWER 3 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-226901 [21] WPIDS

DOC. NO. CPI: C2004-089523

TITLE: New purified thrombospondin fragment extracted from a

body fluid, useful for diagnosing cancer e.g. adenoma, adenocarcinoma, carcinoma, lymphoma or leukemia or as

calibrators, indicators, immunogens and analytes.

DERWENT CLASS: B04 D16

INVENTOR(S): WILLIAMS, K J

PATENT ASSIGNEE(S): (WILL-I) WILLIAMS K J

COUNTRY COUNT: 105

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2004018995 A2 20040304 (200421)\* EN 76

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS

LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH

PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC

VN YU ZA ZM ZW

US 2004053392 A1 20040318 (200421) AU 2003262727 A1 20040311 (200457) US 2005065324 A1 20050324 (200526)

# APPLICATION DETAILS:

| PATENT NO     | KIND           | APPLICATION     | DATE     |
|---------------|----------------|-----------------|----------|
| WO 2004018995 | A2             | WO 2003-US26023 | 20030820 |
| US 2004053392 | Al Provisional | US 2002-405494P | 20020823 |
|               |                | US 2003-419462  | 20030421 |
| AU 2003262727 | A1             | AU 2003-262727  | 20030820 |
| US 2005065324 | Al Provisional | US 2002-405494P | 20020823 |
|               | CIP of         | US 2003-419462  | 20030421 |
|               |                | US 2004-782968  | 20040220 |

#### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2003262727 | Al Based on | WO 2004018995 |

PRIORITY APPLN. INFO: US 2003-419462 20030421; US

2002-405494P 20020823

AN 2004-226901 [21] WPIDS

AB WO2004018995 A UPAB: 20040326

NOVELTY - A purified thrombospondin fragment that has been extracted from a bodily fluid, where the fragment is within a molecular weight range selected from 80--10~kDa, 40--60~kDa or 20--35~kDa, and where the size in kDa is determined by gel electrophoresis after disulfide bond reduction, is new.

DETAILED DESCRIPTION - A thrombospondin fragment or its portion comprising:

- (a) one that starts between amino acyl residues N-230 and G-253 inclusive and ends between amino acyl residues V-400 and S-428;
- (b) one that starts between amino acyl residues N-230 and G-253, inclusive and ends between amino acyl residues D-527 and S-551;
- (c) one that starts between amino acyl residues N-230 and G-253, inclusive and ends between amino acyl residues G-787 and V-811;

- (d) one that starts between amino acyl residues I-165 and V-263, inclusive and ends between amino acyl residues K-412 and 1-530;
- (e) one that starts between amino acyl residues 1-165 and V-263, inclusive, and ends between amino acyl residues 1-530 and R-733;
- (f) one that starts between amino acyl residues 1-165 and V-263, inclusive, and ends between amino acyl residues R-733 and Y-982;
- (g) one that starts between amino acyl residues I-165 and V-263, inclusive, and ends between amino acyl residues K-412 and 1-530;
- (h) one that starts between amino acyl residues 1-165 and V-263, inclusive, and ends between amino acyl residues 1-530 and R-733;
- (i) one that starts between amino acyl residues 1-165 and V-263, inclusive, and ends between amino acyl residues R-792 and Y-982.

The thrombospondin fragment comprises at least 4-6 contiguous amino acyl residues from the thrombospondin sequence, where the amino acid sequence of the fragment is limited to one that is outside of a thrombospondin region given above.

INDEPENDENT CLAIMS are also included for:

- (1) a molecule identical in primary structure to the compound above;
- (2) a method to detect and/or quantify a thrombospondin fragment;
- (3) a method of producing antibodies against a thrombospondin fragment comprising administering the fragment to an organism capable of producing antibodies;
- (4) a monoclonal or polyclonal antibody produced by the method of(3);
- (5) a cell line producing the monoclonal antibodies or the binding agent;
- (6) a method of producing a peptide or non-peptide binding agent against a thrombospondin fragment;
- (7) a kit for the determination of the presence of, and/or the amount of, and/or the concentration of, a thrombospondin fragment in a material taken or gathered from an organism comprising the thrombospondin fragment, a binding agent that will react with thrombospondin but not with the fragment or fragments of interest or an antibody that will react thrombospondin fragments of interest but not with thrombospondin;
- (8) a method comprising determining the amount of the unlabeled or differently labeled fragment through comparison to the results obtained from the unlabeled or differently labeled fragment;
- (9) a method to detect the presence and/or clinical course of a neoplastic disease in an individual; and
- (10) a method of producing a binding agent against a thrombospondin fragment comprising binding a phage to the thrombospondin fragment.
- USE The thrombospondin fragments are useful in diagnostic methods for cancer, as method calibrators, method indicators, as immunogens and as analytes for methods with sustained clinical utility. Cancer is selected from adenoma, adenocarcinoma, carcinoma, lymphoma, leukemia, solid cancer, liquid cancer, metastatic cancer, pre-metastatic cancer, non-metastatic cancer, a cancer with vascular invasion, internal cancer, skin cancer, cancer of the respiratory system, cancer of the circulatory system, cancer of the musculoskeletal system, cancer of a muscle, cancer of a bone, cancer of a joint, cancer of a tendon or ligament, cancer of the digestive system, cancer of the liver or biliary system, cancer of the pancreas, cancer of the head, cancer of the neck, cancer of the endocrine system, cancer of the reproductive system, cancer of the male reproductive system, cancer of the female reproductive system, cancer of the genitourinary system, cancer of a kidney, cancer of the urinary tract, cancer of a sensory system, cancer of the nervous system, cancer of a lymphoid organ, blood cancer, cancer of a gland, cancer of a mammary gland, cancer of a prostate gland, cancer of an endometrial tissue, cancer of a mesodermal tissue, cancer of an ectodermal tissue, cancer of an endodermal tissue, a teratoma, a poorly-differentiated cancer, a well-differentiated cancer, and a moderately differentiated cancer. Dwq.0/4

L3 ANSWER 4 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-011801 [01] WPIDS

DOC. NO. CPI: C2004-003469

TITLE: Selecting an antibody from a phage display library using

sequential antigen panning, useful for treating or reducing infections, such as bacterial, virus and parasitic infection, and for inhibiting cancers.

DERWENT CLASS: B04 D16

INVENTOR(S): DIMITROV, D S; ZHANG, M

PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES; (DIMI-I) DIMITROV

D S; (ZHAN-I) ZHANG M

COUNTRY COUNT: 103

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------|------|------|------|----|----|
|           |      |      |      |    |    |

WO 2003092630 A2 20031113 (200401)\* EN 78

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS

LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL

PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU

ZA ZM ZW

AU 2003237187 A1 20031117 (200442) US 2005123900 A1 20050609 (200541)

# APPLICATION DETAILS:

| PATENT NO                      | KIND           | APPLICATION                       | DATE                 |
|--------------------------------|----------------|-----------------------------------|----------------------|
| WO 2003092630<br>AU 2003237187 | A2<br>A1       | WO 2003-US14292<br>AU 2003-237187 | 20030506<br>20030506 |
| US 2005123900                  | Al Provisional | US 2002-378408P                   | 20030506             |
|                                |                | WO 2003-US14292<br>US 2005-513725 | 20030506<br>20050125 |

#### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               |             |               |
| AU 2003237187 | Al Based on | WO 2003092630 |

PRIORITY APPLN. INFO: US 2002-378408P 20020506; US

2005-513725 20050125

AN 2004-011801 [01] WPIDS AB W02003092630 A UPAB: 20040102

NOVELTY - Selecting an antibody comprising selecting an antibody from a phage display library using sequential antigen panning, is new.

 ${\tt DETAILED}$  <code>DESCRIPTION</code> - <code>INDEPENDENT</code> <code>CLAIMS</code> are also included for the following:

- (1) a sequential antigen panning method for selecting an antibody from a phage display library, comprising selecting phage from a phage display library using a first selecting condition, where the first selecting condition is an antigen at a known concentration, and selecting phage from the phage selected using a second selecting condition that differs from the first selecting conditions, with the proviso that this step can be repeated any number of times, each time using a different selecting conditions;
  - (2) a composition produced using any of the methods;
  - (3) a composition comprising a neutralizing antibody that recognizes

more than one strain of a pathogen;

- (4) an antibody to HIV envelope glycoprotein that can recognize one or more strains of HIV, comprising a 233, 228, 231, 237, 214, 210, 212 or 212 amino acid sequence (SEQ ID NO: 1-8), given in the specification, or their variants that retains the ability to bind to the same epitope to a greater or lesser extent;
  - (5) a fusion protein or conjugate comprising the antibody of (4);
- (6) a composition comprising the antibody of (4), where the toxin is Pseudomonas toxin;
- (7) an isolated or purified nucleic acid molecule comprising a sequence encoding amino acid sequence with SEQ ID NO: 1-6, or its variant that retains the ability to bind to the same epitope to a greater or lesser extent;
  - (8) a vector comprising the isolated or purified nucleic acid of (7);
- (9) a composition comprising the isolated or purified nucleic acid molecule of (7), optionally in the form of a vector;
- (10) a host cell comprising the isolated or purified nucleic acid molecule of (7), optionally in the form of a vector;
- (11) treating, inhibiting or reducing the severity of an infection in an animal, comprising administering an infection-inhibiting amount of a composition comprising an antibody produced by the method, optionally in the form of a fusion protein, where the antibody or fusion protein is optionally encoded in an isolated or purified nucleic acid molecule, which is optionally in the form of a vector and/or optionally contained within a cell, where the infection in the animal is inhibited; and
- (12) inhibiting cancer in a mammal, comprising administering an cancer-inhibiting amount of a composition comprising an antibody produced by the method, optionally in the form of a fusion protein, where the antibody or fusion protein is optionally encoded in an isolated or purified nucleic acid molecule, which is optionally in the form of a vector and/or optionally contained within a cell, where the cancer in the animal is inhibited.

ACTIVITY - Antibacterial; Virucide; Antiparasitic; Protozoacide; Fungicide; Cytostatic.

No biological data given.

MECHANISM OF ACTION - Gene-Therapy.

USE - The methods and compositions of the present invention are useful for treating, inhibiting or reducing the severity of an infection, such as bacterial, virus and parasitic infection, and for inhibiting cancers.

Dwg.0/5

ANSWER 5 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-854115 [79] WPIDS

DOC. NO. CPI:

C2003-241002

TITLE:

Diagnosing and/or treating cancer, such as brain, lymphatic, liver, stomach, testicular, cervical,

endometrial, renal, lung and ovarian cancers, leukemia and melanoma, comprises using soluble MIC polypeptides as markers.

DERWENT CLASS:

B04 D16

INVENTOR(S):

SPIES, T; SPIES, V

PATENT ASSIGNEE(S):

(HUTC-N) HUTCHINSON CANCER RES CENT FRED

COUNTRY COUNT: 103

PATENT INFORMATION:

PATENT NO KIND DATE LA PG WEEK

A2 20031030 (200379)\* EN 98 WO 2003089616

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS

LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003225093 A1 20031103 (200438)

# APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION     | DATE     |
|---------------|------|-----------------|----------|
| WO 2003089616 | A2   | WO 2003-US12299 | 20030422 |
| AU 2003225093 | A1   | AU 2003-225093  | 20030422 |

#### FILING DETAILS:

| PATENT  | NO     | KIN | 1D    |    | I  | PATENT | NO    |
|---------|--------|-----|-------|----|----|--------|-------|
|         |        |     |       |    |    |        |       |
| AU 2003 | 225093 | A1  | Based | on | WO | 200308 | 39616 |

PRIORITY APPLN. INFO: US 2002-374442P 20020422

AN 2003-854115 [79] WPIDS

AB W02003089616 A UPAB: 20031208

NOVELTY - Assaying for cancer in a subject comprises obtaining at least a first sample from a subject suspected of having or being at risk for developing cancer, and assaying for a soluble MIC polypeptide in the sample, where identification of a soluble MIC polypeptide in the sample indicates cancer.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) assaying for cancer in a subject, comprising obtaining a sample from a subject suspected of having or being at risk for developing cancer, assaying for a soluble MIC polypeptide in the sample comprising contacting a sample from the subject with a first antibody attached to a solid support, wherein the first antibody binds to a soluble MIC polypeptide in the sample, and incubating the sample with a second antibody, wherein the second antibody binds to the soluble MIC polypeptide, wherein identification of a soluble MIC polypeptide in the sample indicates cancer;
- (2) treating cancer, comprising detecting cancer in a subject by obtaining a sample from the subject and assaying for a soluble MIC polypeptide in the sample, and administering to the subject chemotherapy, radiation therapy, gene therapy, or hormone therapy;
- (3) diagnosing or prognosing an autoimmune disease or condition in a patient, comprising identifying a patient suspected of having an autoimmune disease or condition, and assaying for a soluble MIC polypeptide in a sample from the patient, wherein identification of a soluble MIC polypeptide in the sample indicates an autoimmune disease or condition;
- (4) kit for diagnosing or prognosing cancer or an autoimmune disease in a patient, comprising, in suitable container means an agent that specifically recognizes all or part of a MIC polypeptide or a nucleic acid encoding a MIC polypeptide, and a positive control that can be used to determine whether the agent is capable of specifically recognizing all or part or a MIC polypeptide or a nucleic acid encoding a MIC polypeptide;
- (5) screening for candidate therapeutic agents for an autoimmune disease, comprising contacting a MIC polypeptide with an NKG2D receptor polypeptide in the presence and absence of a candidate substance, assaying for binding between the MIC polypeptide and the NKG2D receptor in its presence and absence, wherein a reduction of binding in its presence compared to its absence is indicative of a candidate therapeutic agent for an autoimmune disease; and
  - (6) assaying an candidate therapeutic agent for efficacy against an

autoimmune disease, comprising contacting a MIC polypeptide with an NKG2D receptor polypeptide in the presence and absence of the candidate substance, wherein the candidate substance is substantially pure, assaying for binding between the MIC polypeptide and the NKG2D receptor in its presence and absence, wherein a reduction of binding in its presence compared to its absence indicates the candidate substance has the ability to reduce binding between the MIC polypeptide and the NKG2D receptor.

ACTIVITY - Cytostatic; Immunosuppressive; Endocrine-Gen.; Anabolic; Hypertensive; Antipsoriatic; Antirheumatic; Antiarthritic; Antiinflammatory; Dermatological.

No biological data given.

MECHANISM OF ACTION - MIC-Modulator; Gene-Therapy.

No biological data given.

USE - The methods and compositions of the present invention are useful for diagnosing, prognosticating and/or treating cancer, such as brain cancer, lymphatic cancer, liver cancer, stomach cancer, testicular cancer, cervical cancer, ovarian cancer, leukemia, melanoma, head and neck cancer, esophageal cancer, colon cancer, breast cancer, lung cancer, prostate cancer, and renal cancer, and autoimmune diseases such as alopecia, Addison's disease, psoriasis, rheumatoid arthritis and systemic lupus erythematosis. Dwq.0/2

ANSWER 6 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

2003-748337 [70] ACCESSION NUMBER: WPIDS

CROSS REFERENCE: 2003-748311 [70]; 2004-604159 [58]

N2003-599814 DOC. NO. NON-CPI: DOC. NO. CPI: C2003-205213

TITLE: Preventing, treating or managing cancer in a patient

comprises administering to the patient VITAXIN or an antibody or its fragment that competes with VITAXIN for binding to Integrin alphavbeta3 and one or more other

cancer therapies.

B04 D16 S03 DERWENT CLASS:

DORMITZER, M; HEINRICHS, J; KIENER, P; WALSH, W; INVENTOR(S):

WOESSNER, R

PATENT ASSIGNEE(S): (MEDI-N) MEDIMMUNE INC

COUNTRY COUNT: 103

ZM ZW

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------|------|------|------|----|----|
|           |      |      |      |    |    |

WO 2003075957 A1 20030918 (200370) \* EN 155

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS

LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA

US 2004001835 A1 20040101 (200402) AU 2003217930 A1 20030922 (200431) A1 20041222 (200501) EN EP 1487492

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

# APPLICATION DETAILS:

| PATENT NO     | KIND           | APPLICATION     | DATE     |
|---------------|----------------|-----------------|----------|
| WO 2003075957 | Al             | WO 2003-US6684  | 20030304 |
| US 2004001835 | Al Provisional | US 2002-361859P |          |

|    |            |           | Provisional | US | 2002-370398P | 20020405 |
|----|------------|-----------|-------------|----|--------------|----------|
|    |            |           | Provisional | US | 2003-444265P | 20030130 |
|    |            |           |             | US | 2003-379189  | 20030304 |
| ΑU | 2003217930 | A1        |             | AU | 2003-217930  | 20030304 |
| ΕP | 1487492    | <b>A1</b> |             | EP | 2003-713905  | 20030304 |
|    |            |           |             | WO | 2003-US6684  | 20030304 |

#### FILING DETAILS:

| PATENT  | NO | KI | 1D             | <br>I | PATENT | ИО |
|---------|----|----|----------------|-------|--------|----|
| AU 2003 |    |    | Based<br>Based | <br>  | 200307 |    |

PRIORITY APPLN. INFO: US 2003-444265P 20030130; US

> 2002-361859P 20020304; US 2002-370398P 20020405; US 2003-379189 20030304

AN 2003-748337 [70] WPIDS

2003-748311 [70]; 2004-604159 [58] CR

WO2003075957 A UPAB: 20050103 AB

> NOVELTY - Preventing, treating or managing cancer in a patient, comprises administering to the patient VITAXIN (RTM) or its antigen-binding fragment, or an antibody or its fragment that competes with VITAXIN (RTM) for binding to Integrin alpha v beta 3 and a dose of one or more other cancer therapies.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition;

(2) a method of screening for antibodies with specific binding affinity for the epitope specifically recognized by VITAXIN; and

(3) a method for detecting Integrin alpha v beta 3 in tissue.

ACTIVITY - Cytostatic; Fungicide; Antiparasitic; Antiemetic; Antiinflammatory; Virucide. No biological data given.

MECHANISM OF ACTION - Gene therapy; Vaccine.

USE - The method is useful for preventing, treating or managing cancer in a patient (claimed). Dwq.0/7

ANSWER 7 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: DOC. NO. CPI:

2003-167365 [16] C2003-043494

TITLE:

Nanoparticle useful as synthetic vaccine, comprises carrier, and ligands displayed on the carrier, where ligands form polyvalent binding unit to produce

interaction between nanoparticle and receptors on target.

DERWENT CLASS:

B04 C06 D16

INVENTOR(S): BARGATZE, R F; CUTLER, J E; GLEE, P M; HAN, Y; JUTILA, J

W; NAGY, J O; PASCUAL, D

PATENT ASSIGNEE(S):

(BARG-I) BARGATZE R F; (CUTL-I) CUTLER J E; (GLEE-I) GLEE P M; (HANY-I) HAN Y; (JUTI-I) JUTILA J W; (NAGY-I) NAGY J

O; (PASC-I) PASCUAL D; (LIGO-N) LIGOCYTE PHARM INC;

WPIDS

(UYMO-N) UNIV MONTANA STATE-BOZEMAN

COUNTRY COUNT: 97

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------|------|------|------|----|----|
|           |      |      |      |    |    |

WO 2002100325 A2 20021219 (200316) \* EN 56

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO

RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

US 2003223938 A1 20031204 (200380) AU 2001297913 A1 20021223 (200452)

# APPLICATION DETAILS:

| PATENT NO                      | KIND                            | APPLICATION   | DATE                             |
|--------------------------------|---------------------------------|---|----------------------------------|
| WO 2002100325<br>US 2003223938 | A2<br>A1 Provisional<br>Cont of | WO 2001-US42712<br>US 2000-239874P<br>WO 2001-US42712 | 20011015<br>20001013<br>20011015 |
| AU 2001297913                  | A1                              | US 2003-412685<br>AU 2001-297913                      | 20030414<br>20011015             |

#### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               |             |               |
| AU 2001297913 | Al Based on | WO 2002100325 |

PRIORITY APPLN. INFO: US 2000-239874P 20001013; US

2003-412685 20030414

AN 2003-167365 [16] WPIDS

AB WO2002100325 A UPAB: 20030307

NOVELTY - A nanoparticle (I) comprising a carrier, a first ligand (L1), and a second ligand (L2), that is different than L1, both displayed on the carrier, is new. L1 and L2 form a polyvalent binding unit to produce a specific interaction between the nanoparticle and receptor(s) on a target, and L2 interacts specifically with the receptor(s) based on its charge or hydrophobicity.

DETAILED DESCRIPTION - A nanoparticle (I) comprising a carrier, a first ligand (L1), and a second ligand (L2), that is different than L1, both displayed on the carrier, is new. L1 and L2 form a polyvalent binding unit to produce a specific interaction between the nanoparticle and receptor(s) on a target under physiologically relevant shear conditions, and L2 interacts specifically with the receptor(s) based on its charge or hydrophobicity.

INDEPENDENT CLAIMS are also included for the following:

- (1) a therapeutic formulation (II) in unit dose form comprising (I), to modulate a specific interaction between a cell or toxin and its receptor on a target in a host, where L1 is derived from or mimics a ligand on the cell or toxin;
- (2) a vaccine (III) comprising (I), where L1 is an epitope that is derived from a pathogen, pathogen-derived toxin or tumor cell, and the vaccine is formulated to elicit a protective immune response against that pathogen or tumor cell;
- (3) a diagnostic imaging agent comprising (I), and further comprising a contrast agent detectable by medical resonance imaging or other visualization techniques;
- (4) a delivery vehicle (IV) comprising (I), and an agent to be delivered to the target;
- (5) optimizing (V) a nanoparticle displaying polyvalent binding units having L1 and L2, comprises optimizing the amount of L1 on the nanoparticle under physiologically relevant shear conditions and holding the optimized amount of L1 constant, optimizing the amount of L2 under physiologically relevant shear conditions;
- (6) a nanoparticle library (VI) comprising multiple polymer beads, where each bead contains several nanoparticles associated with the surface of the polymer bead, where all of the nanoparticles associated with any one bead display the same polyvalent binding unit;

- (7) a vaccine comprising (I), and a polynucleotide sequence that encodes an epitope found on a pathogen or a tumor cell and the vaccine is formulated to elicit a protective immune response against that pathogen or tumor cell; and
  - (8) a nanoparticle produced by (VI).

ACTIVITY - Antibacterial; Fungicide; Virucide; Protozoacide; Anti-HIV; Immunostimulant; Antiinflammatory; Cytostatic.

MECHANISM OF ACTION - Vaccine; Inhibitor of lymphocyte attachment in Peyer's patch.

A variation on the Peyer's patch method was used to examine the P-selectin-mediated adhesion in a mouse mesentery venule model. A lateral incision was made into the abdominal wall to allow the small intestine to be externalized. The intestine was positioned for microscopic examination of the mesentery. A solution of PMA in phosphate buffered saline was superfused directly onto the mesentery to allow for upregulation of P-selectin in the endothelium of the mesentery venules. The area of the incision was treated and cannulation of the tail vein was performed. A variable dose of carbohydrate— and sulfate—displaying nanoparticle was administered. The results showed the reduction in number of leukocyte rolling and sticking events compared to the untreated control, and the increase in cell velocity relative to the untreated control. At the highest dosage tested (2.3 mg/kg of carbohydrate), there was a greater than 65% reduction in the number of rolling/sticking leukocytes and a nearly 90% increase in the rolling velocity, over the control.

USE - (I) is useful for sequestration of toxins in the bloodstream of a host, by administering (I) to bind a circulating toxin or toxic metabolic product, where the first ligand is derived from or mimics a receptor that specifically binds to the toxin or toxic metabolic product. The binding is effective to produce an effect such as decreased inflammation, decreased systemic toxicity, chelation therapy, neutralization of pathogens, inhibition of metastasis, inhibition of drug intoxication, tissue regeneration, selective cellular differentiation and proliferation. (I) is also useful in a diagnostic method by allowing (I) to bind to a toxin or pathogen or an antibody against such toxins or pathogens and then detecting nanoparticles bound to such toxins, pathogen or antibodies. (III) is formulated to elicit a protective immune response against a pathogen such as Escherichia coli, Candida albicans, Brucella sp., Salmonella sp., Shigella sp., Pseudomonas sp., Bordetella sp., Clostridium sp., group B strep, E.coli 0157, Norwalk virus, anthrax, human immunodeficiency virus (HIV), sexually transmitted diseases (STDs), Chlamydia, hepatitis B virus (HBV), malaria, cell wall proteins of Candida sp., and GB3 toxin from E.coli 0157. (IV) is useful for delivering an agent such as therapeutic or cytotoxic agent to a target. (VI) is useful for screening agents, by adding at least one candidate agent to the nanoparticle library, and detecting binding of the agent to any one or more polymer beads in the library. The candidate agent comprises a detectable label and acts as a reporter to L1. Vaccine construct comprising (I) is useful for delivering nanoparticle therapeutic molecules to an animal (all claimed).

The polymerized nanoparticle constructs and assemblies are useful as modulators, inhibitors and enhancers and drug delivery agents for a variety of interactions as well as their down-stream effects, such as pathogen-cell attachment, pathogen-derived-toxin-cell attachment, cell-cell attachment mediated diseases, integrin adhesions, complement fixation and chemokine-mediated events. The nanoparticles are readily used as synthetic vaccines.

Dwg.0/6

L3 ANSWER 8 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-759837 [82] WPIDS

DOC. NO. CPI: C2002-214753

TITLE: New Major Histocompatibility Complex (MHC) molecule

construct, useful for treating, preventing, stabilizing or alleviating a disease involving MHC recognizing cells

e.g., cancer.

DERWENT CLASS: B04 D16

INVENTOR(S): AMELLEM, O; BUUS, S; PETERSEN, L O; RUUD, E; SCHOLLER, J;

WINTHER, L; AAMELLEM, O; RUUB, E; SCHOELLER, J

PATENT ASSIGNEE(S): (DAKO-N) DAKO AS; (DYNA-N) DYNAL BIOTECH ASA; (DAKO-N)

DAKOCYTOMATION DENMARK AS

COUNTRY COUNT: 101

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2002072631 A2 20020919 (200282)\* EN 304

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM

ΖW

NO 2003004020 A 20031106 (200380)

EP 1377609 A2 20040107 (200404) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI TR

AU 2002240818 A1 20020924 (200433)

JP 2005500257 W 20050106 (200505) 439

#### APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
| WO 2002072631 | A2   | WO 2002-DK169  | 20020313 |
| NO 2003004020 | A    | WO 2002-DK169  | 20020313 |
|               |      | NO 2003-4020   | 20030911 |
| EP 1377609    | A2   | EP 2002-706685 | 20020313 |
|               |      | WO 2002-DK169  | 20020313 |
| AU 2002240818 | A1   | AU 2002-240818 | 20020313 |
| JP 2005500257 | W    | JP 2002-571544 | 20020313 |
|               |      | WO 2002-DK169  | 20020313 |

# FILING DETAILS:

| PA | TENT NO                             | KIN | 1D                      |    | I  | PATENT NO                              |
|----|-------------------------------------|-----|-------------------------|----|----|--|
| AU | 1377609<br>2002240818<br>2005500257 | A1  | Based<br>Based<br>Based | on | WO | 2002072631<br>2002072631<br>2002072631 |

PRIORITY APPLN. INFO: US 2001-275470P 20010314; DK 2001-435 20010314; DK 2001 436

2001-436 20010314; DK 2001-441 20010314; US 2001-275447P 20010314; US

2001-275448P 20010314

AN 2002-759837 [82] WPIDS

AB WO 200272631 A UPAB: 20021220

NOVELTY - A new Major Histocompatibility Complex (MHC) molecule construct comprising a carrier molecule to which one or more MHC molecules are attached either directly or via one or more entities, is new.

 ${\tt DETAILED}$  <code>DESCRIPTION</code> - <code>INDEPENDENT</code> <code>CLAIMS</code> are also included for the following:

- (1) detecting the presence or MHC recognizing cells in a sample;
- (2) monitoring MHC recognizing cells;
- (3) establishing a prognosis of a disease involving MHC recognizing cells;
- (4) determining the status of, or the effectiveness of a medicament against, a disease involving MHC recognizing cells;
  - (5) diagnosing a disease involving MHC recognizing cells;
- (6) a therapeutic composition comprising as active ingredient a MHC molecule construct;
- (7) up-regulating, down-regulating or modulating an immune response in an animal, including a human being;
  - (8) treating an animal, including a human being;
  - (9) inducing energy of a cell in animal, including a human being;
  - (10) an adoptive cellular immunotherapeutic method;
  - (11) obtaining MHC recognizing cells; or
  - (12) producing a therapeutic composition.

ACTIVITY - Cytostatic; Antiinflammatory; Dermatological; Antiasthmatic; Antidiabetic; Anti-HIV; Virucide; Antiarteriosclerotic; Antiulcer; Antirheumatic; Antiarthritic; Antipsoriatic; Immunosuppressive. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - The MHC molecule construct is useful as a therapeutic composition in in vivo or ex vivo therapy, for treating, preventing, stabilizing or alleviating a disease involving MHC recognizing cells, for monitoring MHC recognizing cells or establishing a prognosis of a disease or diagnosing a disease, or determining the status of a disease or the effectiveness of a medicament against a disease, involving MHC recognizing cells, e.g., chronic inflammatory bowel disease such as Crohn's disease or ulcerative colitis, sclerosis, type I diabetes, rheumatoid arthritis, psoriasis, atopic dermatitis, asthma, malignant melanoma, renal carcinoma, breast cancer, lung cancer, cancer of the uterus, cervical cancer, prostate cancer, brain cancer, head and neck cancer, leukemia, cutaneous lymphoma, hepatic carcinoma, colorectal cancer, bladder cancer, rejection-related disease, Graft-versus-host-related disease, or a viral disease associated with hepatitis, Acquired Immunodeficiency Syndrome (AIDS), measles, pox, chicken pox, rubella or herpes. The MHC molecule construct is also useful for flow cytometric, histological or cytological method (all claimed.) Dwg.0/57

L3 ANSWER 10 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 1999-610208 [52] WPIDS

DOC. NO. CPI: C1999-177599

TITLE: Inducing human immunodeficiency virus-specific helper

T-cell responses.

DERWENT CLASS: B04 D16
INVENTOR(S): WALKER, B D

PATENT ASSIGNEE(S): (GEHO) GEN HOSPITAL CORP

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG
-----US 5972339 A 19991026 (199952)\* 25

# APPLICATION DETAILS:

| PATENT NO  | KIND | APPLICATION    | DATE     |
|------------|------|----------------|----------|
|            |      |                |          |
| US 5972339 | Α    | US 1997-969721 | 19971113 |

PRIORITY APPLN. INFO: US 1997-969721 19971113

AN 1999-610208 [52] WPIDS

AB US 5972339 A UPAB: 19991210

NOVELTY - A method (X) for producing human immunodeficiency virus (HIV)-specific helper T-cell responses in animals using helper T-cell epitopes of peptides 112, 117, 118, 120, 121, 122, 125 and/or 127, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the

following:

(i) a method (X) for producing a human immunodeficiency virus (HIV)-specific helper T-cell response in an animal, comprising:

- (1) providing a polypeptide 8 to 50 amino acid residues in length comprising a helper T-cell epitope of the HIV capsid (which produces a stimulation index more than 10 in CD4+ cells in a subject chronically infected with HIV); and
- (2) administering the polypeptide to produce a HIV-specific helper T-cell response; and

(ii) a composition (Y) comprising:

(1) a polypeptide 8 to 50 amino acid residues in length, comprising a helper T-cell epitope of peptide 112, 117, 118, 120, 121, 122, 125 and/or 127 (which have defined amino acid sequences ((I) -(VIII)) given in the specification); and

(2) an adjuvant.

ACTIVITY - Anti-HIV.

MECHANISM OF ACTION - Vaccine.

USE - (X) may be used for inducing HIV-specific helper T-cell responses in animals (preferably humans), especially those already chronically infected with HIV (i.e. inducing immunity by vaccination).  ${\tt Dwg.0/5}$ 

L3 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 1999220994 MEDLINE DOCUMENT NUMBER: PubMed ID: 10206153

TITLE: Plakophilin, armadillo repeats, and nuclear localization.

AUTHOR: Klymkowsky M W

CORPORATE SOURCE: Molecular, Cellular and Developmental Biology, University

of Colorado, Boulder 80309-0347, USA..

klym@spot.colorado.edu

CONTRACT NUMBER: GM54001 (NIGMS)

SOURCE: Microscopy research and technique, (1999 Apr 1) 45 (1)

43-54.

Journal code: 9203012. ISSN: 1059-910X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199907

ENTRY DATE: Entered STN: 19990816

Last Updated on STN: 19990816 Entered Medline: 19990730

AB Plakophilins are armadillo-repeat containing proteins, identified through their localization to desmosomes. Expressed in a wide range of tissues, plakophilins are largely nuclear in most cell types [Schmidt et al. (1997) Cell Tissue Res 290:481; Mertens et al. (1996) J. Cell Biol 135:1009]. Using Xenopus embryos and cultured A6 cells, together with myc- and green fluorescent protein (GFP)-tags, we found that both the N-terminal, non-armadillo repeat "head" and the C-terminal armadillo repeat-containing regions can enter nuclei. The "arm" repeat domain is predominantly cytoplasmic and concentrated at the cell cortex, whereas the head and full-length polypeptides are concentrated in the nucleus. The head domain can also be seen to decorate and disrupt keratin filament network organization in some cells. In the course of these studies, we found that the distribution of the myc-epitope and green fluorescence

differed in fixed cells, e.g., while the green fluorescence of a myc- and GFP-tagged head domain polypeptide was usually exclusively nuclear, a substantial fraction of the myc-immunoreactivity was cytoplasmic. Treating cells with the translation inhibitor cycloheximide reduces the cytoplasmic myc-signal, suggesting that it represented nascent polypeptides awaiting folding and nuclear import. Based on these types of experiments, GFP can be seen as a marker of the distribution of the mature form of the tagged polypeptide.

L3 ANSWER 12 OF 12 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 91107695 MEDLINE DOCUMENT NUMBER: PubMed ID: 1703157

TITLE: Differential localization of two epitopes of Escherichia

coli ribosomal protein L2 on the large ribosomal subunit by

immune electron microscopy using monoclonal antibodies.

AUTHOR: Olson H M; Nag B; Etchison J R; Traut R R; Glitz D G
CORPORATE SOURCE: Department of Biological Chemistry and Molecular Biology

Institute, UCLA School of Medicine, University of

California 90024.

CONTRACT NUMBER: GM 17924 (NIGMS)

GM 32769 (NIGMS)

SOURCE: Journal of biological chemistry, (1991 Jan 25) 266 (3)

1898-902.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199102

ENTRY DATE: Entered STN: 19910329

Last Updated on STN: 19980206 Entered Medline: 19910227

ΔR Two monoclonal antibodies (mAb), directed toward different epitopes of Escherichia coli ribosomal protein L2, have been used as probes in immune electron microscopy. mAb 5-186 recognizes an epitope within residues 5-186 of protein L2; it is seen to bind to 50 S subunits at or near the peptidyl transferase center, beside the subunit head on the L1 shoulder. mAb 187-272 recognizes an epitope within residues 187-272. This antibody binds to the face of the 50 S subunit, below the head and slightly toward the side with the stalk; this site is near the translocation domain. Both antibodies can bind simultaneously to single subunits. This indicates that protein L2 is elongated, reaching from the peptidyl transferase center to below the subunit head and approaching the translocational domain. The different locations of the two epitopes are consistent with previous biochemical results with the two antibodies (Nag, B., Tewari, D. S., Etchison, J. R., Sommer, A., and Traut, R. R. (1986) J. Biol. Chemical 261, 13892-13897).

# => d his

(FILE 'HOME' ENTERED AT 15:58:16 ON 22 JUL 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 15:58:37 ON 22 JUL 2005

L1 10 HEAD (S) DIFFERENT (S) EPITOPE L2 16 HEAD (S) DIFFER? (S) EPITOPE

L3 12 DUP REM L2 (4 DUPLICATES REMOVED)

=> head (s) differ? (s) (ligand or receptor)

L4 288 HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)

- => (head (s) differ? (s) (ligand or receptor)) and tail L5 26 (HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)) AND TAIL
- => dup rem 15
  PROCESSING COMPLETED FOR L5
  L6 15 DUP REM L5 (11 DUPLICATES REMOVED)
- => t ti 16 1-15
- L6 ANSWER 1 OF 15 MEDLINE on STN DUPLICATE 1
- TI Membrane-proximal {alpha}/{beta} stalk interactions differentially regulate integrin activation.
- L6 ANSWER 2 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Determining whether treatment of a disorder with histone deacetylase inhibitors is to be started/continued or not, using antibody capable of binding to acetylated histone but not to deacetylated histone.
- L6 ANSWER 3 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Nanoparticle useful as synthetic vaccine, comprises carrier, and ligands displayed on the carrier, where ligands form polyvalent binding unit to produce interaction between nanoparticle and receptors on target.
- L6 ANSWER 4 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Epitopes formed by non-covalent association of conjugates, useful in therapeutic, prophylactic or diagnostic methods.
- L6 ANSWER 5 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Detecting heterogeneous nucleic acid sequences in organisms and cells, useful for detecting and identifying genetically modified organisms or their products.
- L6 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- Preparation and electrochemical behavior of dinuclear platinum complexes containing NCN ligands (NCN = [C6H3(Me2NCH2)2-2,6]-). The crystal structure of [C6H3(Me2NCH2)2-1,3-(C.tplbond.C)-5]2
- L6 ANSWER 7 OF 15 MEDLINE on STN DUPLICATE 2
- TI The influence of stereoisomerism on the pharmacokinetics of Tc radiopharmaceuticals.
- L6 ANSWER 8 OF 15 MEDLINE on STN DUPLICATE 3
- TI Selective targeting of human cells by a chimeric adenovirus vector containing a modified fiber protein.
- L6 ANSWER 9 OF 15 MEDLINE on STN DUPLICATE 4
- TI Ligand recruitment by vinculin domains in transfected cells.
- L6 ANSWER 10 OF 15 MEDLINE on STN DUPLICATE 5
- TI Synthesis and biological evaluation of a new reversely linked type of dual histamine H2 and gastrin receptor antagonist.
- L6 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Synthesis and Characterization of Poly(benzoyl-1,4-phenylene)s. 2. Catalyst Coligand Effects on Polymer Properties
- L6 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Cytosine nucleobase as a tridentate ligand: metal binding to N(3), N(4) and O(2) in trans-[(NH2Me)2Pt(dmcyt)2Ag2][NO3]2 (dmcyt = 1,5-dimethylcytosinate)

- L6 ANSWER 13 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI CHARACTERIZATION OF 5-HT RECEPTOR SUBTYPES INVOLVED IN THE MOTOR BEHAVIORS PRODUCED BY INTRATHECAL ADMINISTRATION OF 5-HT AGONISTS IN RATS.
- L6 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- X-ray crystal structure and homonuclear phosphorus-31-phosphorus-31  $\sigma/J$ -resolved NMR spectroscopic studies of tetrakis (1,8-diisocyanomethane)bis(triphenylphosphine)diirdium silver(3+) tris(hexafluorophosphate). Observation of a statistical mixture of "head/tail" isomers
- L6 ANSWER 15 OF 15 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
- TI The regional distribution of a morphine like factor enkephalin in monkey brain.

 $\Rightarrow$  d ibib abs 16 1-3, 5

L6 ANSWER 1 OF 15 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2005329024 IN-PROCESS

DOCUMENT NUMBER: PubMed ID: 15863495

TITLE: Membrane-proximal {alpha}/{beta} stalk interactions

differentially regulate integrin activation.

AUTHOR: Kamata Tetsuji; Handa Makoto; Sato Yukiko; Ikeda Yasuo;

Aiso Sadakazu

CORPORATE SOURCE: Departments of Anatomy, Transfusion Medicine and Cell

Therapy, and Internal Medicine, Keio University School of Medicine, Tokyo 160-8582, Japan.. kamata@sc.itc.keio.ac.jp

SOURCE: Journal of biological chemistry, (2005 Jul 1) 280 (26)

24775-83. Electronic Publication: 2005-04-29.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20050628

Last Updated on STN: 20050715

AB The affinity of integrin-ligand interaction is regulated extracellularly by divalent cations and intracellularly by inside-out signaling. We report here that the extracellular, membrane-proximal alpha/beta stalk interactions not only regulate cation-induced integrin activation but also play critical roles in propagating inside-out signaling. Two closely related integrins, alphaIIbbeta3 and alphaVbeta3, share high structural homology and bind to similar ligands in an RGD-dependent manner. Despite these structural and functional similarities, they exhibit distinct responses to Mn(2+). Although alphaVbeta3 showed robust ligand binding in the presence of Mn(2+), alphaIIbbeta3 showed a limited increase but failed to achieve full activation. Swapping alpha stalk regions between alphaIIb and alphaV revealed that the alpha stalk, but not the ligand -binding head region, was responsible for the difference

. A series of alphaIIb/alphaV domain-swapping chimeras were constructed to identify the responsible domain. Surprisingly, the minimum component required to render alphaIIbbeta3 susceptible to Mn(2+) activation was the alphaV calf-2 domain, which does not contain any divalent cation-binding sites. The calf-2 domain makes interface with beta epidermal growth factor 4 and beta tail domain in three-dimensional structure. The effect of calf-2 domain swapping was partially reproduced by mutating the specific amino acid residues in the calf-2/epidermal growth factor 4-beta tail domain interface. When this interface was constrained by an artificially introduced disulfide bridge, the

Mn(2+)-induced alphaVbeta3-fibrinogen interaction was significantly impaired. Notably, a similar disulfide bridge completely abrogated fibrinogen binding to alphaIIbbeta3 when alphaIIbbeta3 was activated by cytoplasmic tail truncation to mimic inside-out signaling. Thus, disruption/formation of the membrane-proximal alpha/beta stalk interface may act as an on/off switch that triggers integrin-mediated bidirectional signaling.

L6 ANSWER 2 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-271984 [26] WPIDS

DOC. NO. NON-CPI: N2004-215240 DOC. NO. CPI: C2004-105664

TITLE: Determining whether treatment of a disorder with histone

deacetylase inhibitors is to be started/continued or not, using antibody capable of binding to acetylated histone

but not to deacetylated histone.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): ARECES, L B; FARETTA, M; MACCARANA, M; MINUCCI, S;

PELICCI, P G; PICCINI, D; RONZONI, S

PATENT ASSIGNEE(S): (GTWO-N) G2M CANCER DRUGS AG

COUNTRY COUNT: 107

PATENT INFORMATION:

| PA | ГЕИТ | NO   |       |    | KI | ND I | TAC  | Ξ   | Ţ   | WEE  | K                |      | LA | ]  | PG |    |    |    |    |    |    |             |    |
|----|------|------|-------|----|----|------|------|-----|-----|------|------------------|------|----|----|----|----|----|----|----|----|----|-------------|----|
| EP | 140  | 363  | <br>9 |    | A1 | 200  | 0403 | 331 | (20 | 0042 | 26) <sup>-</sup> | * E1 | 1  | 36 | -  |    |    |    |    |    |    |             |    |
|    | R:   | AL   | ΑT    | BE | BG | CH   | CY   | CZ  | DΕ  | DK   | EE               | ES   | FI | FR | GB | GR | ΙE | IT | LI | LT | LU | $_{\rm LV}$ | MC |
|    |      | MK   | NL    | PT | RO | SE   | SI   | SK  | TR  |      |                  |      |    |    |    |    |    |    |    |    |    |             |    |
| WO | 200  | 4029 | 9622  | 2  | A2 | 200  | 0404 | 108 | (20 | 0042 | 26)              | Eì   | 1  |    |    |    |    |    |    |    |    |             |    |
|    | RW:  | ΑT   | BE    | BG | CH | CY   | CZ   | DE  | DK  | EΑ   | EE               | ES   | FI | FR | GB | GH | GM | GR | HU | ΙE | IT | ΚE          | LS |
|    |      | LU   | MC    | MW | MZ | NL   | ΟA   | PT  | RO  | SD   | SE               | SI   | SK | SL | SZ | TR | TZ | UG | ZM | ZW |    |             |    |
|    | W:   | ΑE   | AG    | AL | ΑM | AT   | ΑU   | ΑZ  | BA  | BB   | BG               | BR   | BY | BZ | CA | CH | CN | CO | CR | CU | CZ | DE          | DK |
|    |      | DM   | DΖ    | EC | EE | EG   | ES   | FI  | GB  | GD   | GE               | GH   | GM | HR | HU | ID | IL | IN | IS | JΡ | KE | KG          | ΚP |
|    |      | KR   | ΚZ    | LC | LK | LR   | LS   | LT  | LU  | LV   | MA               | MD   | MG | MK | MN | MW | ΜX | MZ | NI | NO | NZ | OM          | PG |
|    |      | PH   | PL    | PT | RO | RU   | SC   | SD  | SE  | SG   | SK               | SL   | SY | ТJ | TM | TN | TR | TT | TZ | UA | UG | US          | UZ |
|    |      | VC   | VN    | YU | ZA | ZM   | ZW   |     |     |      |                  |      |    |    |    |    |    |    |    |    |    |             |    |
| AU | 2003 | 327  | 1663  | 3  | A1 | 200  | 0404 | 119 | (20 | 0046 | 52)              |      |    |    |    |    |    |    |    |    |    |             |    |

EP 1546712 A2 20050629 (200543) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

#### APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION     | DATE     |
|---------------|------|-----------------|----------|
| EP 1403639    | A1   | EP 2002-21984   | 20020930 |
| WO 2004029622 | A2   | WO 2003-EP10842 | 20030930 |
| AU 2003271663 | A1   | AU 2003-271663  | 20030930 |
| EP 1546712    | A2   | EP 2003-753482  | 20030930 |
|               |      | WO 2003-EP10842 | 20030930 |

#### FILING DETAILS:

| PATENT NO                   | KIND                    | PATENT NO                      |
|-----------------------------|-------------------------|--------------------------------|
| AU 2003271663<br>EP 1546712 | Al Based on A2 Based on | WO 2004029622<br>WO 2004029622 |

PRIORITY APPLN. INFO: EP 2002-21984 20020930

AN 2004-271984 [26] WPIDS

AB EP 1403639 A UPAB: 20040421

NOVELTY - Determining (M1) whether treatment of disorder with histone

deacetylase (HDAC) inhibitor is to be started/continued/not by contacting sample from tissue affected by disorder with antibody binding to acetylated histone but not to deacetylated histone, determining histone level acetylation in sample and classifying disorder as to be treated with HDAC inhibitor when histone acetylation level is significantly less than control sample.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) use of an antibody capable of binding to acetylated histone for determining whether a treatment of a disorder with an HDAC inhibitor is to be started/continued or not, and/or the classification of tumors;
- (2) an antibody (I) capable of binding to peptides having a sequence of Ser-Gly-Arg-Gly-Lys-Gly-Lys-Gly-Leu-Gly-Lys-Gly-Gly-Ala-Lys- Arg (histone H4 tail, mono-acetylated at lysine 8) (S1) and Ser-Gly-Arg-Gly-Lys-Gly-Lys-Gly-Leu-Gly-Lys-Gly-Gly-Ala-Lys- Arg (histone H4 tail, mono-acetylated at lysine 12) (S2) but not to anyone of the peptides having the sequences of Ser-Gly-Arg-Gly-Lys-Gly-Gly-Lys-Gly-Lys-Gly-Lys-Gly-Ala-Lys- Arg (histone H4 tail, mono-acetylated at lysine 16) (S3), Ser-Gly-Arg-Gly-Lys-Gly-Gly-Lys-Gly-Leu-Gly-Lys-Gly-Ala-Lys- Arg (non-acetylated peptide) (S4), Ala-Val-Cys-Asp-Lys-Cys-Leu-Lys-Phe-Tyr-Ser-Lys and Val-Trp-Asp-Gln-Glu-Phe-Leu-Lys-Val-Asp-Gln-Gly;
- (3) an antibody (II) capable of binding to peptides having (S1), (S2) and (S3) but not to peptides having (S4);
- (4) an antibody produced by a hybridoma cell line chosen from hybridoma cell lines G2M-T25-H4ac and G2M-T52-ac deposited at DSMZ;
  - (5) a hybridoma cell line producing (I) or (II);
- (6) a hybridoma cell line which has the identifying characteristics of the cell line G2M-T25-H4ac deposited at DSMZ;
- (7) a hybridoma cell line which has the identifying characteristics of the cell line G2M-T52-ac deposited at DSMZ;
- (8) a diagnostic kit (III) for determining the level of histone acetylation containing an antibody capable of binding to acetylated histone but not to deacetylated histone, an HDAC inhibitor, and optionally, a secondary antibody directed against the antibody, and optionally reagents for the measurement of a signal derived from an antibody binding to acetylated histones; and
- (9) use of the antibodies T25 and/or T52 (IV) to direct substances conjugated to these antibodies to sites of histone hyperacetylation.
- USE (M1) is useful for determining whether a treatment of a disorder with an HDAC inhibitor is to be started/continued or not. The disorder is chosen from diseases in which the induction of hyperacetylation of histones has a beneficial effect resulting in differentiation and/or apoptosis of a patient's tumor cells, diseases that show aberrant recruitment of HDAC activity, conditions associated with abnormal gene expression, autoimmune diseases, and proliferative diseases such as skin cancer, melanoma, estrogen receptor-dependent and independent breast cancer, ovarian cancer, testosterone receptor-dependent and independent prostate cancer, renal cancer, colon and colorectal cancer, pancreatic cancer, bladder cancer, esophageal cancer, stomach cancer, genitourinary cancer, gastrointestinal cancer, uterine cancer, astrocytomas, gliomas, basal cancer and squamous cell carcinoma, sarcomas as Kaposi's sarcoma and osteosarcoma, head and neck cancer, small cell and non-small cell lung carcinoma, leukemia, lymphomas and other blood cell cancers or thyroid resistance syndrome (claimed). Dwg.0/11

L6 ANSWER 3 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN ACCESSION NUMBER: 2003-167365 [16] WPIDS

DOC. NO. CPI: C2003-043494

TITLE: Nanoparticle useful as synthetic vaccine, comprises carrier, and ligands displayed on the carrier, where

ligands form polyvalent binding unit to produce

interaction between nanoparticle and receptors on target.

DERWENT CLASS: B04 C06 D16

INVENTOR(S):

BARGATZE, R F; CUTLER, J E; GLEE, P M; HAN, Y; JUTILA, J

W; NAGY, J O; PASCUAL, D

PATENT ASSIGNEE(S):

(BARG-I) BARGATZE R F; (CUTL-I) CUTLER J E; (GLEE-I) GLEE P M; (HANY-I) HAN Y; (JUTI-I) JUTILA J W; (NAGY-I) NAGY J O; (PASC-I) PASCUAL D; (LIGO-N) LIGOCYTE PHARM INC;

(UYMO-N) UNIV MONTANA STATE-BOZEMAN

COUNTRY COUNT: 97

PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LΑ | PG |
|-----------|-----------|------|----|----|
|           |           |      |    |    |

WO 2002100325 A2 20021219 (200316)\* EN 56

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO

RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

US 2003223938 A1 20031204 (200380) AU 2001297913 A1 20021223 (200452)

#### APPLICATION DETAILS:

| PATE | ENT NO     | KINI | )                      | Al | PPLICATION                   | DATE                 |
|------|------------|------|------------------------|----|------------------------------|----------------------|
|      | 2002100325 | A2   |                        |    | 2001-US42712                 | 20011015             |
| US 2 | 2003223938 | A1   | Provisional<br>Cont of |    | 2000-239874P<br>2001-US42712 | 20001013<br>20011015 |
|      |            |      | Cont or                |    | 2001-0342712                 | 20031414             |
| AU 2 | 2001297913 | A1   |                        | AU | 2001-297913                  | 20011015             |

#### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               |             |               |
| AU 2001297913 | Al Based on | WO 2002100325 |

PRIORITY APPLN. INFO: US 2000-239874P 20001013; US

2003-412685 20030414

AN 2003-167365 [16] WPIDS

AB W02002100325 A UPAB: 20030307

NOVELTY - A nanoparticle (I) comprising a carrier, a first ligand (L1), and a second ligand (L2), that is different than L1, both displayed on the carrier, is new. L1 and L2 form a polyvalent binding unit to produce a specific interaction between the nanoparticle and receptor(s) on a target, and L2 interacts specifically with the receptor(s) based on its charge or hydrophobicity.

DETAILED DESCRIPTION - A nanoparticle (I) comprising a carrier, a first ligand (L1), and a second ligand (L2), that is different than L1, both displayed on the carrier, is new. L1 and L2 form a polyvalent binding unit to produce a specific interaction between the nanoparticle and receptor(s) on a target under physiologically relevant shear conditions, and L2 interacts specifically with the receptor(s) based on its charge or hydrophobicity.

INDEPENDENT CLAIMS are also included for the following:

(1) a therapeutic formulation (II) in unit dose form comprising (I), to modulate a specific interaction between a cell or toxin and its receptor on a target in a host, where L1 is derived from or mimics a ligand on the cell or toxin;

- (2) a vaccine (III) comprising (I), where L1 is an epitope that is derived from a pathogen, pathogen-derived toxin or tumor cell, and the vaccine is formulated to elicit a protective immune response against that pathogen or tumor cell;
- (3) a diagnostic imaging agent comprising (I), and further comprising a contrast agent detectable by medical resonance imaging or other visualization techniques;
- (4) a delivery vehicle (IV) comprising (I), and an agent to be delivered to the target;
- (5) optimizing (V) a nanoparticle displaying polyvalent binding units having L1 and L2, comprises optimizing the amount of L1 on the nanoparticle under physiologically relevant shear conditions and holding the optimized amount of L1 constant, optimizing the amount of L2 under physiologically relevant shear conditions;
- (6) a nanoparticle library (VI) comprising multiple polymer beads, where each bead contains several nanoparticles associated with the surface of the polymer bead, where all of the nanoparticles associated with any one bead display the same polyvalent binding unit;
- (7) a vaccine comprising (I), and a polynucleotide sequence that encodes an epitope found on a pathogen or a tumor cell and the vaccine is formulated to elicit a protective immune response against that pathogen or tumor cell; and
  - (8) a nanoparticle produced by (VI).

ACTIVITY - Antibacterial; Fungicide; Virucide; Protozoacide; Anti-HIV; Immunostimulant; Antiinflammatory; Cytostatic.

MECHANISM OF ACTION - Vaccine; Inhibitor of lymphocyte attachment in Peyer's patch.

A variation on the Peyer's patch method was used to examine the P-selectin-mediated adhesion in a mouse mesentery venule model. A lateral incision was made into the abdominal wall to allow the small intestine to be externalized. The intestine was positioned for microscopic examination of the mesentery. A solution of PMA in phosphate buffered saline was superfused directly onto the mesentery to allow for upregulation of P-selectin in the endothelium of the mesentery venules. The area of the incision was treated and cannulation of the tail vein was performed. A variable dose of carbohydrate- and sulfate-displaying nanoparticle was administered. The results showed the reduction in number of leukocyte rolling and sticking events compared to the untreated control, and the increase in cell velocity relative to the untreated control. At the highest dosage tested (2.3 mg/kg of carbohydrate), there was a greater than 65% reduction in the number of rolling/sticking leukocytes and a nearly 90% increase in the rolling velocity, over the control.

USE - (I) is useful for sequestration of toxins in the bloodstream of a host, by administering (I) to bind a circulating toxin or toxic metabolic product, where the first ligand is derived from or mimics a receptor that specifically binds to the toxin or toxic metabolic product. The binding is effective to produce an effect such as decreased inflammation, decreased systemic toxicity, chelation therapy, neutralization of pathogens, inhibition of metastasis, inhibition of drug intoxication, tissue regeneration, selective cellular differentiation and proliferation. (I) is also useful in a diagnostic method by allowing (I) to bind to a toxin or pathogen or an antibody against such toxins or pathogens and then detecting nanoparticles bound to such toxins, pathogen or antibodies. (III) is formulated to elicit a protective immune response against a pathogen such as Escherichia coli, Candida albicans, Brucella sp., Salmonella sp., Shigella sp., Pseudomonas sp., Bordetella sp., Clostridium sp., group B strep, E.coli 0157, Norwalk virus, anthrax, human immunodeficiency virus (HIV), sexually transmitted diseases (STDs), Chlamydia, hepatitis B virus (HBV), malaria, cell wall proteins of Candida sp., and GB3 toxin from E.coli 0157. (IV) is useful for delivering an agent such as therapeutic or cytotoxic agent to a target. (VI) is useful

for screening agents, by adding at least one candidate agent to the nanoparticle library, and detecting binding of the agent to any one or more polymer beads in the library. The candidate agent comprises a detectable label and acts as a reporter to L1. Vaccine construct comprising (I) is useful for delivering nanoparticle therapeutic molecules to an animal (all claimed).

The polymerized nanoparticle constructs and assemblies are useful as modulators, inhibitors and enhancers and drug delivery agents for a variety of interactions as well as their down-stream effects, such as pathogen-cell attachment, pathogen-derived-toxin-cell attachment, cell-cell attachment mediated diseases, integrin adhesions, complement fixation and chemokine-mediated events. The nanoparticles are readily used as synthetic vaccines.

Dwg.0/6

L6 ANSWER 5 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-098663 [14] WPIDS

DOC. NO. CPI: C2002-030908

TITLE: Detecting heterogeneous nucleic acid sequences in

organisms and cells, useful for detecting and identifying

genetically modified organisms or their products.

DERWENT CLASS: B04 D16

INVENTOR(S): BERNAUER, H; BERNAUER, H S

PATENT ASSIGNEE(S): (BERN-I) BERNAUER H; (BERN-I) BERNAUER H S

COUNTRY COUNT: 97

PATENT INFORMATION:

| PA | TENT | ИО   |            |    | KII | I DV | DATI          | Ξ   | 1   | WEE  | K   |    | LΑ | 1  | PG |    |    |    |    |    |    |    |    |
|----|------|------|------------|----|-----|------|---------------|-----|-----|------|-----|----|----|----|----|----|----|----|----|----|----|----|----|
|    | 100  |      |            |    |     |      |               |     | •   |      |     |    |    | 11 | -  |    |    |    |    |    |    | -  |    |
| "" |      |      |            |    |     |      |               |     | •   |      | •   |    |    |    |    |    |    |    |    |    |    |    |    |
|    | RW:  | AT   | $_{ m BE}$ | CH | CY  | DE   | DK            | EΑ  | ES  | FI   | FR  | GB | GH | GM | GR | ΙE | IT | KE | LS | LU | MC | MW | MZ |
|    |      | NL   | OA         | PT | SD  | SE   | $\mathtt{SL}$ | SZ  | TR  | TZ   | UG  | ZW |    |    |    |    |    |    |    |    |    |    |    |
|    | W:   | ΑE   | AG         | AL | AM  | ΑT   | ΑU            | ΑZ  | BA  | BB   | BG  | BR | BY | BZ | CA | CH | CN | CO | CR | CU | CZ | DE | DK |
|    |      | DM   | DZ         | EC | EE  | ES   | FI            | GB  | GD  | GE   | GH  | GM | HR | HU | ID | IL | IN | IS | JР | KE | KG | KP | KR |
|    |      | ΚZ   | LC         | LK | LR  | LS   | LT            | LU  | LV  | MA   | MD  | MG | MK | MN | MW | ΜX | ΜZ | NO | NZ | PL | PT | RO | RU |
|    |      | SD   | SE         | SG | SI  | SK   | $\mathtt{SL}$ | TJ  | TM  | TR   | TT  | TZ | UΑ | UG | US | UZ | VN | YU | ZA | zw |    |    |    |
| ΑU | 200  | 1070 | 0545       | 5  | Α   | 200  | 020           | L02 | (20 | 0023 | 30) |    |    |    |    |    |    |    |    |    |    |    |    |
| ΕP | 1315 | 5834 | 4          |    | A2  | 200  | 306           | 504 | (20 | 003  | 37) | GI | Ξ  |    |    |    |    |    |    |    |    |    |    |
|    | R:   | AL   | ΑT         | BE | СН  | CY   | DE            | DK  | ES  | FI   | FR  | GB | GR | ΙE | IT | LI | LT | LU | LV | MC | MK | NL | PT |

#### APPLICATION DETAILS:

| PATENT NO                                     | KIND          | APPLICATION   | DATE                             |
|---|---------------|---|----------------------------------|
| DE 10027218<br>WO 2001098533<br>AU 2001070545 | A1<br>A2<br>A | DE 2000-10027218<br>WO 2001-EP6198<br>AU 2001-70545 | 20000531<br>20010531<br>20010531 |
| EP 1315834                                    | A2            | EP 2001-949371<br>WO 2001-EP6198                    | 20010531<br>20010531             |

# FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2001070545 | A Based on  | WO 2001098533 |
| EP 1315834    | A2 Based on | WO 2001098533 |

PRIORITY APPLN. INFO: DE 2000-10027218 20000531

AN 2002-098663 [14] WPIDS AB DE 10027218 A UPAB: 20020301

RO SE SI TR

NOVELTY - Simultaneously detecting one or more heterogeneous nucleic acids (I), introduced into organisms and cells, where (I) includes at least one artificial sequence (II) that allows both determination of the identity of (I) and selective replication, and (II) are detected, and optionally identified, by hybridization to a chip and/or by sequencing, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a chip for use in the new process.

USE - The method is used (i) for detection/identification of genetically modified organisms and vectors (or their products), e.g. in foods or for detecting improper use and (ii) for correlating phenotypical features with particular regions of chromosomes.

ADVANTAGE - This method provides simple, rapid, inexpensive and unequivocal identification and detection of genetically modified organisms and vectors. (II) can be detected independently of the type of construct containing it. Dwg.0/2

SINCE FILE

TOTAL

=> FIL STNGUIDE COST IN U.S. DOLLARS

ENTRY SESSION 114.94

FULL ESTIMATED COST 115.15

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FILE CONTAINS CURRENT INFORMATION. LAST RELOADED: Jul 15, 2005 (20050715/UP).

=> fil medline biosis caplus embase wpids

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 0.24 115.39

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=> amphipathic and tail and (head (s) conjugat?) O AMPHIPATHIC AND TAIL AND (HEAD (S) CONJUGAT?)

=> tail and (head (s) conjugat?) 113 TAIL AND (HEAD (S) CONJUGAT?)

=> (bilayer or membrane) and tail and (head (s) conjugat?) 24 (BILAYER OR MEMBRANE) AND TAIL AND (HEAD (S) CONJUGAT?)

=> dup rem 19

=> t ti 110 1-11

L10 ANSWER 1 OF 11 MEDLINE on STN DUPLICATE 1

TI Protein circlets as sex pilus subunits.

L10 ANSWER 2 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

TI Liposome useful for treating angiogenesis comprises a conjugate containing a vesicle-forming lipid and a non-biological, biomimetic antagonist, bound to its lipid bilayer.

L10 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

FI Crystal structure of 9-(hexadecyl)imino-4,5-diazafluorene

L10 ANSWER 4 OF 11 MEDLINE on STN DUPLICATE 2

TI Conjugates of synthetic cyclic peptides elicit bactericidal antibodies against a conformational epitope on a class 1 outer membrane protein of Neisseria meningitidis.

L10 ANSWER 5 OF 11 MEDLINE on STN DUPLICATE 3

II Binding of metallothionein to rat spermatozoa.

L10 ANSWER 6 OF 11 MEDLINE on STN DUPLICATE 4

TI Relationship between fertilizing ability of frozen human spermatozoa and capacity for heparin binding and nuclear decondensation.

L10 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

TI MEMBRANE SPECIALIZATIONS IN THE PAIRED SPERMATOZOA OF DYTISCID WATER BEETLES.

L10 ANSWER 8 OF 11 MEDLINE on STN DUPLICATE 5

TI Distinct cytoskeletal domains revealed in sperm cells.

L10 ANSWER 9 OF 11 MEDLINE on STN DUPLICATE 6

TI The features of sperm maturation in the epididymis of a marsupial, the brushtailed possum Trichosurus vulpecula.

L10 ANSWER 10 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

TI The features of sperm maturation in the epididymis of a marsupial, the brushtailed possum Trichosurus vulpecula.

L10 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

TI Molecular probes of spermatozoan structures

 $\Rightarrow$  d ibib abs 110 2,4,

L10 ANSWER 2 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-666793 [71] WPIDS

DOC. NO. CPI: C2002-187111

TITLE: Liposome useful for treating angiogenesis comprises a

conjugate containing a vesicle-forming lipid and a

non-biological, biomimetic antagonist, bound to its lipid

bilayer.

DERWENT CLASS: A96 B05 B07

INVENTOR(S): ELLENS, H M; MONCK, M A; YEH, P

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (ELLE-I) ELLENS H M;

(MONC-I) MONCK M A; (YEHP-I) YEH P

COUNTRY COUNT: 98

#### PATENT INFORMATION:

| PA | rent | NO   |      |    | KII | ND 1 | DATI          | Ε             | 7   | WEE  | K                |       | LA    | 1  | PG |            |    |    |    |    |    |    |    |
|----|------|------|------|----|-----|------|---------------|---------------|-----|------|------------------|-------|-------|----|----|------------|----|----|----|----|----|----|----|
| WO | 200  | 203  | 6073 | 3  | A2  | 200  | 020           | 510           | (20 | 002  | 71) <sup>3</sup> | <br>E | ٦<br> | 44 | -  |            |    |    |    |    |    |    |    |
|    | RW:  | ΑT   | BE   | CH | CY  | DE   | DK            | EA            | ES  | FI   | FR               | GB    | GH    | GM | GR | ΙE         | IT | KE | LS | LU | MC | MW | ΜZ |
|    |      | NL   | OA   | PT | SD  | SE   | $\mathtt{SL}$ | SZ            | TR  | TZ   | UG               | ZW    |       |    |    |            |    |    |    |    |    |    |    |
|    | W:   | ΑE   | AG   | AL | ΑM  | ΑT   | ΑU            | ΑZ            | BA  | ВВ   | BG               | BR    | BY    | ΒZ | CA | CH         | CN | CO | CR | CU | CZ | DE | DK |
|    |      | DM   | DZ   | EC | EE  | ES   | FI            | GB            | GD  | GE   | GH               | GM    | HR    | HU | ID | IL         | IN | IS | JP | KE | KG | ΚP | KR |
|    |      | ΚZ   | LC   | LK | LR  | LS   | LT            | LU            | r   | MA   | MD               | MG    | MK    | MN | MW | MX         | ΜZ | ИО | ΝZ | PH | PL | PT | RO |
|    |      | RU   | SD   | SE | SG  | SI   | SK            | $\mathtt{SL}$ | TJ  | TM   | TR               | TT    | TZ    | UA | UG | US         | UZ | VN | YU | ZA | ZW |    |    |
| AU | 200  | 2025 | 5878 | 3  | Α   | 200  | 0205          | 515           | (20 | 002  | 71)              |       |       |    |    |            |    |    |    |    |    |    |    |
| EP | 134  | 149  | 7    |    | A2  | 200  | 0309          | 910           | (20 | 003  | 57)              | Εì    | 1     |    |    |            |    |    |    |    |    |    |    |
|    | R:   | AL   | ΑT   | ΒE | CH  | CY   | DE            | DK            | ES  | FI   | FR               | GB    | GR    | ΙE | ΙT | $_{ m LI}$ | LT | LU | LV | MC | MK | NL | PT |
|    |      | RO   | SE   | SI | TR  |      |               |               |     |      |                  |       |       |    |    |            |    |    |    |    |    |    |    |
|    | 200  |      |      |    |     | 200  | 0401          | 122           | (20 | 004  | 07)              |       |       |    |    |            |    |    |    |    |    |    |    |
| JP | 2004 | 1512 | 2345 | 5  | W   | 200  | 0404          | 122           | (20 | 0042 | 28)              |       |       | 81 |    |            |    |    |    |    |    |    |    |

#### APPLICATION DETAILS:

| PATENT NO                      | KIND    | APPLICATION                        |                      |  |  |  |  |  |
|--------------------------------|---------|------------------------------------|----------------------|--|--|--|--|--|
| WO 2002036073<br>AU 2002025878 | A2<br>A | WO 2001-US46206                    | 20011029             |  |  |  |  |  |
| EP 1341497                     | A<br>A2 | AU 2002-25878<br>EP 2001-992551    | 20011029<br>20011029 |  |  |  |  |  |
| US 2004013720                  | A1      | WO 2001-US46206<br>WO 2001-US46206 | 20011029<br>20011029 |  |  |  |  |  |
| JP 2004512345                  | W       | US 2003-415160<br>WO 2001-US46206  | 20030425<br>20011029 |  |  |  |  |  |
|                                |         | JP 2002-538885                     | 20011029             |  |  |  |  |  |

#### FILING DETAILS:

| PATENT NO                   | KIND                   | PATENT NO                      |
|-----------------------------|------------------------|--------------------------------|
| AU 2002025878<br>EP 1341497 | A Based on A2 Based on | WO 2002036073<br>WO 2002036073 |
| JP 2004512345               | W Based on             | WO 2002036073                  |

PRIORITY APPLN. INFO: US 2000-245140P 20001102; US 2003-415160 20030425

AN 2002-666793 [71] WPIDS AB WO 200236073 A UPAB: 20030813

NOVELTY - A liposome comprises a **conjugate** bound to its lipid **bilayer**. The **conjugate** comprises a vesicle-forming lipid having a polar **head** group and a hydrophobic **tail**, and a non-biological, biomimetic antagonist (A1) to a receptor upregulated at a disease site, directly or indirectly chemically linked to the polar **head** group of the vesicle-forming lipid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) The conjugate useful for preparing a targeted liposomes; and
- (2) Use of the liposome in the manufacture of a medicament in the treatment of a disease caused by upregulation of the receptor.

ACTIVITY - Vasotropic; osteopathic; antiarthritic; anti-rheumatic; anti-diabetic; antipsoriatic; and cytostatic.

MECHANISM OF ACTION - In vitro alpha  $\nu$  beta 3 and alpha  $\nu$  beta 5 binder.

Distearaylphosphatidylethanolamine-polyethylene glycol-vitronectin receptor antagonist (DSPE-PEG-VRA) was synthesized by reacting (7-((4-amino-butyl)-(1H-benzoimidazol-2-ylmethyl)-carbamoyl)-4-methyl-3-oxo-2,3,4,5-tetrahydro-1H-benzo(e)(1,4)diazepin-2-yl)-acetic acid (VRA)

(50 mg) with DSPE-PEG-NHS in DMSO (10 ml). Excess amount of VRA (1.2 times molar excess) was used. The VRA was completely dissolved in DMSO. DSPE-PEG-NHS pre-dissolved in DMSO was added dropwise to the VRA solution. The resulting reaction mixture was stirred overnight in the dark at room temperature. The unreacted DSPE-PEG-NHS was quenched by the addition of excess glycine (5 times molar excess). The reaction mixture was diluted with 0.1M MES (morpholino ethenesulfonic acid) saline buffer (pH 5.8) and then dialyzed against the MES buffer (pH 5.8) to remove by-product, DMSO, and unreacted VRA. At this point the unreacted DSPG-PEG-NHS was hydrolyzed into DSPE-PEG-COOH. The resulting mixture was then dialyzed and lyophilized to form DSPE-PEG-VRA (VRA-lipid conjugate) (A). A liposome (L1) was tested for its binding affinity to human alpha v beta 3 or alpha v beta 5 using an in vitro solid phase binding assay described by Wong A, Hwang SM, McDevitt P, McNulty D, Stadel JM and Johanson K, studies on alpha v beta 3/ligand interaction using a (3H) SK and F-107260 binding assay (1996) Molecular pharmacology 50 (3):529 - 537. A control composition comprised cholesterol (40), PEG3400 DSPE (pegylated DSPE) (7) and POPC (53) was tested for the same binding test as that of the test conjugate. The binding affinity Ki (nm) of the test/control composition was 31/no binding effect.

USE - In the manufacture of a medicament for the treatment of diseases caused by upregulation of integrin and vitronectin receptor e.g. angiogenesis including restenosis, osteoarthritis, rheumatoid arthritis, diabetic retinopathy, hemangiomas, psoriasis and cancerous tumor (all claimed).

ADVANTAGE - The antagonist has binding affinity to the upregulation receptor, which is upregulated in the vascular endothelium of inflammation, infection or tumor sites. Dwg.0/0

L10 ANSWER 4 OF 11 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 95369902 MEDLINE DOCUMENT NUMBER: PubMed ID: 7543883

TITLE: Conjugates of synthetic cyclic peptides elicit bactericidal

antibodies against a conformational epitope on a class 1

outer membrane protein of Neisseria meningitidis.

AUTHOR: Hoogerhout P; Donders E M; van Gaans-van den Brink J A;

Kuipers B; Brugghe H F; van Unen L M; Timmermans H A; ten

Hove G J; de Jong A P; Peeters C C; +

CORPORATE SOURCE: Laboratory of Vaccine Development and Immune Mechanisms,

National Institute of Public Health and Environmental

Protection, Bilthoven, The Netherlands.

SOURCE: Infection and immunity, (1995 Sep) 63 (9) 3473-8.

Journal code: 0246127. ISSN: 0019-9567.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199509

ENTRY DATE: Entered STN: 19950930

Last Updated on STN: 19960129 Entered Medline: 19950921

AB Bactericidal antibodies directed against surface loops of class 1 outer membrane proteins play a crucial role in protection against meningitis and sepsis caused by Neisseria meningitidis. So far, all efforts to obtain protective antibodies against these apparently conformational epitopes by using linear peptide analogs have been in vain. In this study, conjugates of head-to-tail cyclic peptides encompassing the predicted top of a protective surface loop were used for immunization. A series of 18 cyclic peptides with a ring size ranging from 7 to 17 residues, conjugated to tetanus toxoid, was investigated. Antipeptide and anti-whole-cell immunoglobulin G (IgG)

titers elicited by the conjugates were determined. Conjugates of three peptides, containing 14, 15, and 17 amino acid residues (peptides 7, 12, and 13, respectively), induced an anti-whole-cell titer when Quillaja saponin A was used as the adjuvant. When alum was used as the adjuvant, the conjugate of peptide 12 did not elicit an anti-whole-cell response. From the Quillaja saponin A group, some of the sera obtained with conjugates of peptides 7 and 12 and all sera obtained with the peptide 13 conjugate were bactericidal in vitro. None of the sera evoked with alum as the adjuvant showed bactericidal activity. Nonbactericidal sera contained IgG1 primarily, whereas bactericidal sera showed significant titers of IgG2a and IgG2b. Class 1 protein-derived synthetic cyclic peptides which are capable of eliciting bactericidal antibodies, such as peptide 13 derived from meningococcal strain H44/76, represent potential candidates for a (semi)synthetic vaccine against meningococcal disease.

=> FIL STNGUIDE COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 38.62 154.01

FULL ESTIMATED COST

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FILE CONTAINS CURRENT INFORMATION. LAST RELOADED: Jul 15, 2005 (20050715/UP).

=> d his

(FILE 'HOME' ENTERED AT 15:58:16 ON 22 JUL 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 15:58:37 ON 22 JUL 2005

L110 HEAD (S) DIFFERENT (S) EPITOPE L2

16 HEAD (S) DIFFER? (S) EPITOPE

L3 12 DUP REM L2 (4 DUPLICATES REMOVED)

L4288 HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)

L5 26 (HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)) AND TAIL

L6 15 DUP REM L5 (11 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 16:09:56 ON 22 JUL 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 16:12:12 ON 22 JUL 2005

L7 O AMPHIPATHIC AND TAIL AND (HEAD (S) CONJUGAT?)

L8113 TAIL AND (HEAD (S) CONJUGAT?)

24 (BILAYER OR MEMBRANE) AND TAIL AND (HEAD (S) CONJUGAT?)

11 DUP REM L9 (13 DUPLICATES REMOVED)

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=> fil medline biosis caplus embase wpids

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 0.72 154.73

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=> 18 not 19 L11 89 L8 NOT L9

=> dup rem 111
PROCESSING COMPLETED FOR L11
L12 75 DUP REM L11 (14 DUPLICATES REMOVED)

=> t ti 112 1-50

- L12 ANSWER 1 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Nucleic acid strand invasion to destabilize double-stranded nucleic acid hybridization comprises utilizing uracil-DNA glycosylase or an enzyme comprising a DNA N-glycosylase activity.
- L12 ANSWER 2 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

  TI Isolated or synthesized composition, useful for diagnosing and treating bladder disorders and cancer, comprises urinary bladder antiproliferative factor having sugar moieties linked to hydrophobic moiety.
- L12 ANSWER 3 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
  TI Polymeric conductive composition used to modify charge transport across nanocrystal surface, comprises functionalized head group capable of binding to nanostructure surface.
- L12 ANSWER 4 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN TI Knife bayonet.
- L12 ANSWER 5 OF 75 MEDLINE on STN DUPLICATE 1
  TI New insight into solvent effects on the formal HOO\* + HOO\* reaction.
- L12 ANSWER 6 OF 75 MEDLINE on STN DUPLICATE 2
  TI Effect of structural factors on the stability of duplexes formed by
- oligonucleotide conjugates with minor groove binders.
- L12 ANSWER 7 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Effect of structural factors on the stability of duplexes formed by oligonucleotide conjugates with minor groove binders
- L12 ANSWER 8 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
- TI Organic species that facilitate charge transfer to or from nanostructures
- L12 ANSWER 9 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
- TI Combinatorial library of cyclic peptides as antibacterial agents .
- L12 ANSWER 10 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Injectable liposomal composition for delivery of a water-soluble substance e.g. vaccine for preventing pregnancy, comprises several liposomal vesicles comprising a high weight ratio of lipid to encapsulated water-soluble substance.

- L12 ANSWER 11 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

  TI Galvanic cell, e.g. microbattery, has cathode and anode having respective vesicle comprising benzoquinone or hydroquinone, electroactive species encapsulated into the vesicles, conducting substrate, and functionalized
- vesicle comprising benzoquinone or hydroquinone, electroactive species encapsulated into the vesicles, conducting substrate, and functionalized tethers.
- L12 ANSWER 12 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Method reducing bottom resistance of artillery projectile and gear for its implementation.
- L12 ANSWER 13 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Alkyl-substituted thieno[3,2-b]thiophene polymers and their dimeric subunits
- L12 ANSWER 14 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Cobalt-catalyzed dimerization of alkenes
- L12 ANSWER 15 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Direct observation of the ordering and molecular folding of poly[(m-phenylenevinylene)-co-(2,5-dioctyloxy-p-phenylenevinylene)]
- L12 ANSWER 16 OF 75 MEDLINE on STN DUPLICATE 5
- TI A high-spin and durable polyradical: poly(4-diphenylaminium-1,2-phenylenevinylene).
- L12 ANSWER 17 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Solvatochromic, thermochromic and photoluminescent properties of poly(3-octylthiophene)
- L12 ANSWER 18 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Soft propylene resin composition for films and sheets comprises stereoblock propylene polymer containing isotactic block, and propylene-ethylene copolymer.
- L12 ANSWER 19 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Preparation of vulcanizable composition for tire tread comprises forming premix including processing aids and rubber and mixing premix with carbon black.
- L12 ANSWER 20 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Immobilization of electroactive polymerized vesicles to conducting substrate in electrode of microbattery comprises allowing suspension of vesicles to contact substrate in the presence of functionalized tether.
- L12 ANSWER 21 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- Alpha-olefin terpolymer comprises aliphatic alpha-olefins, and vinyl aromatic monomers optionally substituted by alkyl radicals, and contains block(s) of three vinyl aromatic monomers in head-tail-tail insertion fashion.
- L12 ANSWER 22 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Frolov's bullet.
- L12 ANSWER 23 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Percussive-indexing mechanism.
- L12 ANSWER 24 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Regioregular Head-to-Tail Poly(4-alkylquinoline)s: Synthesis, Characterization, Self-Organization, Photophysics, and Electroluminescence of New n-Type Conjugated Polymers
- L12 ANSWER 25 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN

- TI On the structural effects of the head-to-tail coupled oligo(3-alkylthiophenes) on their optical properties
- L12 ANSWER 26 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Generating a modified protein with reduced antigenicity for treating cancer, AIDS, autoimmune diseases, comprises identifying a protein region antigenic in the first subject using antiserum from either the first or a second subject.
- L12 ANSWER 27 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New n-type polythiophene composition for fabricating thin film field effect transistors.
- L12 ANSWER 28 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Bullet of sporting gun cartridge for rifled weapon.
- L12 ANSWER 29 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Poly(1,2-phenylenevinylene) Ferromagnetically 3,5-Bearing Phenoxyl Radicals
- L12 ANSWER 30 OF 75 MEDLINE on STN DUPLICATE 6
- Design and synthesis of a 256-membered pi-conjugated oligomer library of regionegular head-to-tail coupled quater(3-arylthiophene)s.
- L12 ANSWER 31 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
- TI Epitopes formed by non-covalent association of conjugates
- L12 ANSWER 32 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Sequence Length Distributions (Microstructure) of Regioregular Poly(3-alkylthiophene)s and Related Conjugated Polymers and Their Use in Simulating  $\pi$ - $\pi$ \* Absorption Peak Profiles
- L12 ANSWER 33 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Poly(3-phenylgalvinoxylthiophene). A new conjugated polyradical with high spin concentration
- L12 ANSWER 34 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Undular jump in open-channel flow over a sill
- L12 ANSWER 35 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Preparation and characterization of regionegular head-to-tail  $\pi$ -conjugated poly(pyridine-2,5-diyl)s
- L12 ANSWER 36 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Use of asialo-glycoproteins for treating liver disease, e.g. viral hepatitis, and targeting a glycoprotein to a hepatocyte.
- L12 ANSWER 37 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Grinding head.
- L12 ANSWER 38 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Copolymer of aromatic vinyl, olefin, and non-conjugated diene having improved mechanical strength, elasticity and transparency.
- L12 ANSWER 39 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Ferromagnetic Spin Alignment in Head-to-**Tail** Coupled Oligo(1,4-phenyleneethynylene)s and Oligo(1,4-phenylenevinylene)s Bearing Pendant p-Phenylenediamine Radical Cations
- L12 ANSWER 40 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Two-dimensional crystals of poly(3-alkylthiophene)s: direct visualization

of polymer folds in submolecular resolution

- L12 ANSWER 41 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Preparation of Conjugated Gels of Regioregular HT Sexi(3-n-octylthiophene) and Related Star Molecules
- L12 ANSWER 42 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI  $\pi$ -Conjugated polymers prepared by organometallic polycondensation and metal complexes of the polymers
- L12 ANSWER 43 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Regioregular polymerization of 3-semifluoroalkylthiophenes.
- L12 ANSWER 44 OF 75 MEDLINE on STN DUPLICATE 8
- TI Synthesis of a single-tailed cationic lipid and investigation of its transfection.
- L12 ANSWER 45 OF 75 MEDLINE on STN DUPLICATE 9
- TI The Xenopus Emx genes identify presumptive dorsal telencephalon and are induced by head organizer signals.
- L12 ANSWER 46 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Lubricating oil for mitigating sludge formation in engine oil contains a minor amount of alkyl substituted hydroxy aromatic compound formed by alkylation of ethylene -alpha-olefin copolymer.
- L12 ANSWER 47 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Synthesis and characterization of poly[3-(butylthio)thiophene]: a regioregular head-to-tail polymer
- L12 ANSWER 48 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Use of nucleic acid ligands in flow cytometry
- L12 ANSWER 49 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10
- TI Living Polymerization of (o-(Trimethylsilyl)phenyl)acetylene by Molybdenum Imido Alkylidene Complexes
- L12 ANSWER 50 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Solvent effect on the bathochromic shifts of push-pull dihexylbithiophenes with head-to-head and head-to-tail orientations
- => t ti 112 51-75
- L12 ANSWER 51 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Electroluminescence of regioregular poly(alkylthiophenes)
- L12 ANSWER 52 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Thiophene:alkylthiophene copolymers from substituted dialkyloligothiophenes
- L12 ANSWER 53 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI A dramatic conjugational interchange in the regionegular polythiophene, HT-poly(3-[2,5,8-trioxanonyl]thiophene) via a chemoselective recognition response
- L12 ANSWER 54 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Mercurophilic 1-(8,8-dicyanoheptafulven-3-yl)aza-15-crown-5 ether. Synthesis, x-ray structural analysis, and fixation of its derivative on a polymer
- L12 ANSWER 55 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN

- TI The effect of stereoregularity on the structure of poly(octylthiophene): an x-ray diffraction study
- L12 ANSWER 56 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Site-specific immunoconjugates
- L12 ANSWER 57 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Conducting polymers from anodic coupling of some regiochemically defined dialkoxy-substituted thiophene oligomers
- L12 ANSWER 58 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI The tuning of conjugation by recipe: the synthesis and properties of random head-to-tail poly(3-alkylthiophene) copolymers
- L12 ANSWER 59 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Polymeric nonlinear optical material contains functional gps. at both ends which can form hydrogen bond in head-to-tail form, and does not cause relaxation or orientation.
- L12 ANSWER 60 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Synthesis and physical properties of self-orienting head-to-tail polythiophenes
- L12 ANSWER 61 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Toward tuning electrical and optical properties in conjugated polymers using side-chains: highly conductive head-to-tail, heteroatom functionalized polythiophenes
- L12 ANSWER 62 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Low-temperature magnetic properties for poly(3-alkylthiophenes) and poly(4,4'-dialkyl-2,2'-bithiophenes)
- L12 ANSWER 63 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Polyazomethine conjugated polymer film with second-order nonlinear optical properties fabricated by electric-field-assisted chemical vapor deposition
- L12 ANSWER 64 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Reactions proceeding via the reactive intermediate  $\alpha\text{-vinyl-p-}$  xylylene. Contrasting orientations in the formation of cyclic dimers and polymer
- L12 ANSWER 65 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Structural and quantitative analysis of surface modified poly(vinylidene fluoride) films using ATR FT-IR spectroscopy
- L12 ANSWER 66 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Variable teeth angle reamer has calibrating section with land widening from head to tail end while front angle of teeth decreases.
- L12 ANSWER 67 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Improving colour of aromatic thermoplastic polymer by treatment with peroxy cpd..
- L12 ANSWER 68 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI The Michael induced Ramberg-Baecklund homologation to conjugated isoprenoids
- L12 ANSWER 69 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Electroinitiated polymerization through acetylene and nitrile group bonds
- L12 ANSWER 70 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN

- TI Thermal and radiation-induced dehydrochlorination of poly(vinyl chloride). II. Head-to-head structures
- L12 ANSWER 71 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Structure and stereochemistry of nucleic acid components and their reaction products. III. Crystal structure of the potassium salt of N-(purin-6-ylcarbamoyl)-L-threonine. Possible role of hypermodified bases adjacent to anticodon in codon-anticodon interaction
- L12 ANSWER 72 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Polymer microstructure
- L12 ANSWER 73 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Molecular-orbital theory of reactivity in radical polymerization. II
- L12 ANSWER 74 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Long-chain acids. I. Extension of the isoprene rule
- L12 ANSWER 75 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Cordless tyre with tread of ethylene/propylene/diene terpolymer, and sidewall of segmented copolyester.

=> d ibib abs 112 44,48,56

L12 ANSWER 44 OF 75 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 1999459173 MEDLINE DOCUMENT NUMBER: PubMed ID: 10528072

TITLE: Synthesis of a single-tailed cationic lipid and

investigation of its transfection.

AUTHOR: Tang F; Hughes J A

CORPORATE SOURCE: University of Florida, College of Pharmacy, Department of

Pharmaceutics, Gainesville, FL 32610, USA.

CONTRACT NUMBER: PO1-AG10485 (NIA)

R29-H 1 55779

SOURCE: Journal of controlled release : official journal of the

Controlled Release Society, (1999 Dec 6) 62 (3) 345-58.

Journal code: 8607908. ISSN: 0168-3659.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199912

ENTRY DATE: Entered STN: 20000113

Last Updated on STN: 20000113 Entered Medline: 19991216

AB Single-tailed cationic lipids were originally reported to have low transfection efficiency and high toxicity in plasmid delivery. We hypothesized that particular single-tailed cationic lipids may also function in plasmid transfection. To test this hypothesis, we synthesized a new cationic lipid-oleoyl ornithinate (OLON). To decrease cytotoxicity, we then introduced a potential biodegradable ester bond in the tail of lipid yielding 6-lauroxyhexyl ornithinate (LHON). The data demonstrated that the cytotoxicity of LHON was lower than that of 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP) or OLON. To investigate the transfection activity of the new lipids and determine the cellular uptake of DNA/liposome complexes, we compared the transfection of liposomes produced from double-tailed 1',2'-dioleyl-sn-glycero-3'-succinyl-1, 6-hexanediol ornithine conjugate (DOGSHDO) with an ornithine headgroup, single-tailed OLON with an ornithine head group, double-tailed DOTAP with quaternary amine group, and single-tailed cetyltrimethylammonium bromide (CTAB) with a quaternary amine group. At

the optimal ratios as defined in transfection experiments, OLON/DOPE had more than 10 times the transgene expression than other liposomes even though the DNA uptake was not necessarily greater. In the experiments comparing the release of DNA from DNA/liposome complexes by anionic substances, a greater fraction of DNA was released from DNA/OLON/DOPE complexes than that from DNA/DOTAP/DOPE complexes.

L12 ANSWER 48 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:145215 CAPLUS

DOCUMENT NUMBER: 126:141764

TITLE: Use of nucleic acid ligands in flow cytometry INVENTOR(S): Davis, Ken; Jayasena, Sumedha; Gold, Larry

PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA; Becton Dickinson

and Company

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: 127

PATENT INFORMATION:

| PA'     | PATENT NO. |     |      |     |     |     |      |      |     | ICAT |      |       |     | D   | ATE  |      |     |
|---------|------------|-----|------|-----|-----|-----|------|------|-----|------|------|-------|-----|-----|------|------|-----|
| WO      | WO 9641019 |     |      |     |     |     |      |      |     |      |      |       |     | 1   | 9960 | 530  |     |
|         | W:         | AL, | AM,  | AT, | ΑU, | ΑZ, | BB,  | BG,  | BR, | BY,  | CA,  | CH,   | CN, | CZ, | DE,  | DK,  | EE, |
|         |            | ES, | FI,  | GB, | GE, | HU, | IS,  | JP,  | KE, | KG,  | KP,  | KR,   | ΚZ, | LK, | LR,  | LS,  | LT, |
|         |            | LU, | LV,  | MD, | MG, | MK, | MN,  | MW,  | MX, | NO,  | NZ,  | PL,   | PT, | RO, | RU,  | SD,  | SE, |
|         |            | SG, | SI   |     |     |     |      |      |     |      |      |       |     |     |      |      |     |
|         | RW:        | ΚE, | LS,  | MW, | SD, | SZ, | UG,  | ΑT,  | BE, | CH,  | DE,  | DK,   | ES, | FI, | FR,  | GB,  | GR, |
|         |            | ΙE, | IT,  | LU, | MC, | NL, | PT,  | SE,  | BF, | ΒJ,  | CF,  | CG,   | CI, | CM, | GA,  | GN,  | ML  |
|         | 5853       |     |      |     |     |     |      |      |     |      |      |       |     |     |      |      |     |
|         | 9661       |     |      |     |     |     |      |      |     |      |      |       |     |     |      |      |     |
| EP      | 8322       | 99  |      |     | A1  |     | 1998 | 0410 |     | EP 1 | 996- | 9190  | 17  |     | 1    | 9960 | 530 |
|         | R:         | ΑT, | BE,  | CH, | DE, | DK, | ES,  | FR,  | GB, | GR,  | IT,  | LI,   | LU, | NL, | SE,  | MC,  | PT, |
|         |            | ΙE, |      |     |     |     |      |      |     |      |      |       |     |     |      |      |     |
| AU      | 7737       | 41  |      |     | В2  |     | 2004 | 0603 |     | AU 2 | 001- | 1825  | 7   |     | 2    | 0010 | 202 |
| AU      | 7738       | 15  |      |     | В2  |     |      | 0610 |     |      |      |       |     |     |      | 0010 |     |
| PRIORIT | Y APP      | LN. | INFO | .:  |     |     |      |      |     |      |      |       |     |     |      | 9950 |     |
|         |            |     |      |     |     |     |      |      |     |      |      |       |     |     |      | 9900 |     |
|         |            |     |      |     |     |     |      |      |     |      |      |       |     |     |      | 9910 |     |
|         |            |     |      |     |     |     |      |      |     |      | 991- |       |     |     |      | 9910 |     |
|         |            |     |      |     |     |     |      |      |     |      |      |       |     |     |      | 9921 |     |
|         |            |     |      |     |     |     |      |      |     |      | 994- |       |     |     |      | 9940 |     |
|         |            |     |      |     |     |     |      |      |     |      |      |       |     |     |      | 9940 |     |
|         |            |     |      |     |     |     |      |      |     |      | 996- |       |     |     |      | 9960 |     |
|         |            |     |      |     |     |     |      |      |     |      |      |       |     |     |      | 9960 |     |
|         |            |     |      |     |     |     |      |      | 1   | AU 1 | 996- | 6161: | 1   | 7   | 43 1 | 9960 | 604 |

AB This invention discloses the use of SELEX-developed high-affinity oligonucleotide ligands in flow cytometry diagnostic applications. Specifically, DNA ligands having one or more fluorophore mols. attached are disclosed which are useful in flow cytometry.

L12 ANSWER 56 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:83878 CAPLUS

DOCUMENT NUMBER: 124:172723

TITLE: Site-specific immunoconjugates

AUTHOR(S): Werlen, R. C.; Lankinen, M.; Smith, A.; Chernushevich,

I.; Standing, K. G.; Blakey, D. C.; Shuttleworth, H.;

Melton, R. G.; Offord, R. E.; Rose, K.

CORPORATE SOURCE: Dep. Biochim. Med., Centre Med. Univ., Geneca,

CH-1211, Switz.

SOURCE: Tumor Targeting (1995), 1(5), 251-8

CODEN: TUTAF9; ISSN: 1351-8488

PUBLISHER: Chapman & Hall

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review and discussion with 19 refs. The conjugation of two proteins with different activities in order to get a conjugate with a new hybrid activity is a field of intense investigation. The standard way of preparing such

conjugates uses random acylation of lysine side-chains with heterobifunctional reagents, leading to a mixture of conjugates where both protein partners are linked to one another in different orientations. To circumvent this difficulty, we are developing precise conjugation techniques for the preparation of site-specific protein conjugates. Here we review the preparation, characterization and the use of three such site-specific immunoconjugates: an antibody fragment-enzyme conjugate designed for ADEPT (antibody-directed enzyme prodrug therapy) and two F(ab')3 constructions prepared with different linkers. The ADEPT

conjugate is a head-to-tail conjugate

between an F(ab')3 antibody fragment and the enzyme carboxypeptidase G2 (CPG2). The components are linked through the formation of a hydrazone bond between a carbohydrazide, introduced at the C-terminus of the truncated heavy chain of the antibody fragment by reverse proteolysis, and an aldehyde, obtained by mild periodate oxidation of a threonine introduced at the N-terminus of the CPG2 by genetic engineering. This conjugate has been characterized by ESI-TOF (electrospray ionization time of flight) mass spectrometry and its in vitro and in vivo behavior was compared with that of a corresponding random conjugate. For the preparation of both F(ab')3 constructions, an Fab with a single thiol group was first prepared by digestion with appropriate proteases. In the first case, the thiol was then converted to an aminooxy group. A trivalent construct was then obtained by polyoxime formation with a trialdehyde template. This F(ab')3 has been characterized by ESI-TOF mass spectrometry and its biodistribution in tumor-bearing mice has been investigated. The second F(ab')3 was obtained starting with the same Fab, but the trivalent construct was prepared on a template containing two aldehydes and a maleimide group, allowing the introduction of three Fab in three different steps.

### => d his

(FILE 'HOME' ENTERED AT 15:58:16 ON 22 JUL 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 15:58:37 ON 22 JUL 2005

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L1 10 HEAD (S) DIFFERENT (S) EPITOPE
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- L2 16 HEAD (S) DIFFER? (S) EPITOPE
- L3 12 DUP REM L2 (4 DUPLICATES REMOVED)
- L4 288 HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)
- L5 26 (HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)) AND TAIL
- L6 15 DUP REM L5 (11 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 16:09:56 ON 22 JUL 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 16:12:12 ON 22 JUL 2005

- L7 0 AMPHIPATHIC AND TAIL AND (HEAD (S) CONJUGAT?)
- L8 113 TAIL AND (HEAD (S) CONJUGAT?)
- L9 24 (BILAYER OR MEMBRANE) AND TAIL AND (HEAD (S) CONJUGAT?)
- L10 11 DUP REM L9 (13 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 16:16:53 ON 22 JUL 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 16:24:09 ON 22 JUL 2005

L11 89 L8 NOT L9

L12 75 DUP REM L11 (14 DUPLICATES REMOVED)

=> (bilayer or membrane) and (head (s) conjugat?)

L13 87 (BILAYER OR MEMBRANE) AND (HEAD (S) CONJUGAT?)

=> 113 not 19

L14 63 L13 NOT L9

=> dup rem 114

PROCESSING COMPLETED FOR L14

L15 38 DUP REM L14 (25 DUPLICATES REMOVED)

=> t ti 115 1-38

- L15 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Formulations, conjugates, and combinations of drugs for the treatment of neoplasms
- L15 ANSWER 2 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New anti-tumor and cobalamin conjugate comprising cobalamin or its derivatives or analogue, linker and anti-tumor drug to treat tumor related disorder or disease e.g. Hodgkin's disease, neurofibromatosis and cervical dysplasia.
- L15 ANSWER 3 OF 38 MEDLINE on STN DUPLICATE 1
- TI Preferred conformations of endogenous cannabinoid ligand anandamide.
- L15 ANSWER 4 OF 38 MEDLINE on STN DUPLICATE 2
- TI In vivo and in vitro reconstitution of atg8 conjugation essential for autophagy.
- L15 ANSWER 5 OF 38 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
- TI Macaque sperm release ESP13.2 and PSP94 during capacitation: The absence of ESP13.2 is linked to sperm-zona recognition and binding.
- L15 ANSWER 6 OF 38 MEDLINE on STN DUPLICATE 3
- TI Distal cationic poly(ethylene glycol) lipid conjugates in large unilamellar vesicles prepared by extrusion enhance liposomal cellular uptake.
- L15 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
- TI Human monoclonal antibodies specific to prostate specific membrane antigen (PSMA) for cancer diagnosis and therapy
- L15 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Humanized murine anti-epithelial glycoprotein 1 (EGP-1) antibodies RS7 and conjugates for diagnosis and treatment of cancer
- L15 ANSWER 9 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Enhancement of transport of biological agent, e.g. antifungal agent, across membrane, comprising use of conjugate containing biological agent and oligomer with guanidino or amidino side chains.
- L15 ANSWER 10 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New colloidal carrier composition useful for e.g. passive targeting of drugs to sites of pathology, comprises active agent and lipid-polymer conjugate comprising amphiphilic lipid and polymer e.g. poly-(amino acid derivative).

- L15 ANSWER 11 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New lipid polymer conjugate useful for e.g. vesicular bilayer systems for use e.g. in therapy, comprises e.g. poly-amino acid derivative or poly-amino acid analogue polymer, and lipid attached to nitrogen or carbon terminal of polymer.
- L15 ANSWER 12 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New isolated or recombinant Bcl-B nucleic acids and polypeptides, for treating a disorder associated with apoptosis, such as cell degenerative or proliferative disorder e.g. cancer, Alzheimer's disease or Parkinson's disease.
- L15 ANSWER 13 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Biocompatible material useful for e.g. controlling cellular growth comprises at least two component surface.
- L15 ANSWER 14 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Composition comprising a combination of an oxidizing and/or reducing agent, a protein-denaturing agent, and a hapten, useful for treating neoplasms, tumors, and cancers.
- L15 ANSWER 15 OF 38 MEDLINE on STN
- TI Orienting otolith-ocular reflexes in the rabbit during static and dynamic tilts and off-vertical axis rotation.
- L15 ANSWER 16 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New membrane permanent peptide complexes for medical imaging, diagnostics and therapy.
- L15 ANSWER 17 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Polymeric assay film for direct colorimetric detection of small molecules such as pathogens.
- L15 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Effect of PEG-lipid conjugates on the phase behavior of phosphatidylethanolamine dispersions
- L15 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Receptor membranes.
- L15 ANSWER 20 OF 38 MEDLINE on STN
- TI Otolith and semicircular canal contributions to the human binocular response to roll oscillation.
- L15 ANSWER 21 OF 38 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 5
- TI Determination of imazethapyr using capillary column flow injection liposome immunoanalysis.
- L15 ANSWER 22 OF 38 MEDLINE on STN
- TI Lectin binding characteristics of squamous cell carcinomas of the head and neck.
- L15 ANSWER 23 OF 38 MEDLINE on STN DUPLICATE 6
- TI Evidence for a direct action of GH on haemopoietic cells of a marine fish, the gilthead sea bream (Sparus aurata).
- L15 ANSWER 24 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Ink-jet recording head with uniform conjugation of the second.

- L15 ANSWER 25 OF 38 MEDLINE on STN DUPLICATE 7
- TI Lipid-amphotericin B complex structure in solution: a possible first step in the aggregation process in cell membranes.
- L15 ANSWER 26 OF 38 MEDLINE on STN
- TI [Clinical evaluation of otolithic function by the measurement of ocular cyclotorsion and skew deviation].

  Evaluation clinique de la fonction otolithique par mesure de la cyclotorsion oculaire et de la "skew deviation".
- L15 ANSWER 27 OF 38 MEDLINE on STN DUPLICATE 8
- TI Induction of vesicle-to-micelle transition by bile salts for DOPE vesicles incorporating immunoglobulin G.
- L15 ANSWER 28 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Receptor membrane for bio-sensors comprising a closely packed array of self-assembling amphiphilic molecules having ion channels and/or receptor molecules.
- L15 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Differential localization of glycoconjugates having affinity for concanavalin A on the surface of the sperm head in the testis, the epididymis, and the ejaculate of the ram
- L15 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI pH-dependent stability and fusion of liposomes combining protonatable double-chain amphiphiles with phosphatidylethanolamine
- L15 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Identifying regions of membrane proteins in contact with phospholipid head groups: covalent attachment of a new class of aldehyde lipid labels to cytochrome c oxidase
- L15 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Localization of carbohydrate components in human synovial lining cells by binding with fluoresceinated lectins and their digestion with neuraminidase
- L15 ANSWER 33 OF 38 MEDLINE on STN DUPLICATE 9
- TI Immunocytochemical localization of acrosin in boar spermatozoa.
- L15 ANSWER 34 OF 38 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
- TI Immunocytochemical localization of acrosin in boar spermatozoa.
- L15 ANSWER 35 OF 38 MEDLINE on STN
- TI Branching pattern and properties of vertical- and horizontal-related excitatory vestibuloocular neurons in the cat.
- L15 ANSWER 36 OF 38 MEDLINE on STN DUPLICATE 10
- TI A novel approach for the topographical localization of glycolipids on the cell surface.
- L15 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 11
- TI Physiological studies on the sperm surface component responsible for sperm-egg bonding in sea urchin fertilization. II. Effect of concanavalin A on the fertilizing capacity of sperm
- L15 ANSWER 38 OF 38 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
- TI Ultrasonic tomography in obstetrics and gynecology: Experimental results and clinical methods.

 $\Rightarrow$  d ibib abs 1,9-11,13-15,17-19,25,27-31,36 115

L15 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:216611 CAPLUS

DOCUMENT NUMBER: 142:291340

TITLE: Formulations, conjugates, and combinations of drugs

for the treatment of neoplasms

INVENTOR(S):
Nichols, James M.; Foley, Michael A.; Keith, Curtis;

Padval, Mahesh; Elliott, Peter

PATENT ASSIGNEE(S): Combinatorx, Incorporated, USA

SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT       | NO.  |      |     | KIN | D   | DATE  |       | i   | APPL | ICAT:     | ION 1 | . OV    |     |      | ATE  |     |
|--------------|------|------|-----|-----|-----|-------|-------|-----|------|-----------|-------|---------|-----|------|------|-----|
| WO 2005      | 0209 | 13   |     | A2  | _   | 2005  | 0310  | Ī   | WO 2 | <br>004-1 | JS27  | <br>695 |     |      |      |     |
| W:           | ΑE,  | AG,  | AL, | AM, | AT, | AU,   | AZ,   | BA, | BB,  | BG,       | BR,   | BW,     | BY, | BZ,  | CA,  | CH, |
|              | CN,  | CO,  | CR, | CU, | CZ, | DE,   | DK,   | DM, | DZ,  | EC,       | EE,   | EG,     | ES, | FI,  | GB,  | GD, |
|              | GE,  | GH,  | GM, | HR, | HU, | ID,   | IL,   | IN, | IS,  | JP,       | ΚE,   | KG,     | KP, | KR,  | KZ,  | LC, |
|              | LK,  | LR,  | LS, | LT, | LU, | LV,   | MA,   | MD, | MG,  | MK,       | MN,   | MW,     | MX, | MZ,  | NA,  | NI, |
|              | NO,  | ΝZ,  | OM, | PG, | PH, | PL,   | PT,   | RO, | RU,  | SC,       | SD,   | SE,     | SG, | SK,  | SL,  | SY, |
|              | ТJ,  | TM,  | TN, | TR, | TT, | TZ,   | UA,   | UG, | US,  | UZ,       | VC,   | VN,     | YU, | ZA,  | ZM,  | ZW  |
| RW:          | BW,  | GH,  | GM, | KE, | LS, | MW,   | MZ,   | NA, | SD,  | SL,       | SZ,   | TZ,     | UG, | ZM,  | ZW,  | AM, |
|              | AZ,  | BY,  | KG, | ΚZ, | MD, | RU,   | ТJ,   | TM, | AT,  | BE,       | BG,   | CH,     | CY, | CZ,  | DE,  | DK, |
|              | EE,  | ES,  | FI, | FR, | GB, | GR,   | HU,   | ΙE, | IT,  | LU,       | MC,   | NL,     | PL, | PT,  | RO,  | SE, |
|              | SI,  | SK,  | TR, | BF, | ВJ, | CF,   | CG,   | CI, | CM,  | GΑ,       | GN,   | GQ,     | GW, | ML,  | MR,  | NE, |
|              | SN,  | TD,  | TG  |     |     |       |       |     |      |           |       |         |     |      |      |     |
| US 2005      | 0800 | 75   |     | A1  |     | 2005  | 0414  | Ţ   | US 2 | 004-9     | 92583 | 35      |     | 2    | 0040 | 325 |
| PRIORITY APE | LN.  | INFO | . : |     |     |       |       | Ţ   | US 2 | 003-4     | 1976: | 17P     | ]   | P 20 | 0030 | 325 |
| OTHER SOURCE | (S): |      |     | MAR | TAS | 142:2 | 29134 | 10  |      |           |       |         |     |      |      |     |

AB The invention provides formulations and structural modifications for phenothiazine compds. which result in altered biodistribution, thereby reducing the occurrence of adverse reactions associated with this class of drug.

L15 ANSWER 9 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-558976 [52] WPIDS

DOC. NO. CPI: C2003-150616

TITLE: Enhancement of transport of biological agent, e.g.

antifungal agent, across membrane, comprising

use of conjugate containing biological agent and oligomer

with guanidino or amidino side chains.

DERWENT CLASS: B05

INVENTOR(S): JESSOP, T C; PATTABIRAMAN, K; PELKEY, E T; ROTHBARD, J B;

WENDER, P A

PATENT ASSIGNEE(S): (JESS-I) JESSOP T C; (PATT-I) PATTABIRAMAN K; (PELK-I)

PELKEY E T; (ROTH-I) ROTHBARD J B; (WEND-I) WENDER P A; (CELL-N) CELLGATE INC; (STRD) UNIV LELAND STANFORD JUNIOR

COUNTRY COUNT: 103

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------|------|------|------|----|----|
|           |      |      |      |    |    |

WO 2003049772 A2 20030619 (200352)\* EN 58

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW

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W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

US 2003185788 A1 20031002 (200365)
AU 2002359679 A1 20030623 (200420)
US 2004161405 A9 20040819 (200455)
EP 1461084 A2 20040929 (200463) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC
```

## APPLICATION DETAILS:

| PATENT NO     | KIND           | APPLICATION     | DATE     |
|---------------|----------------|-----------------|----------|
| WO 2003049772 | A2             | WO 2002-US39698 | 20021211 |
| US 2003185788 | Al Provisional | US 2001-339696P | 20011211 |
|               |                | US 2002-318278  | 20021211 |
| AU 2002359679 | A1             | AU 2002-359679  | 20021211 |
| US 2004161405 | A9 Provisional | US 2001-339696P | 20011211 |
|               |                | US 2002-318278  | 20021211 |
| EP 1461084    | A2             | EP 2002-794232  | 20021211 |
|               | •              | WO 2002-US39698 | 20021211 |

#### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2002359679 | Al Based on | WO 2003049772 |
| EP 1461084    | A2 Based on | WO 2003049772 |

PRIORITY APPLN. INFO: US 2001-339696P 20011211; US 2002-318278 20021211

MK NL PT RO SE SI SK TR

AN 2003-558976 [52] WPIDS

AB W02003049772 A UPAB: 20030813

NOVELTY - The transport of a compound across a biological membrane is enhanced by contacting the membrane with a conjugate containing the biological agent covalently attached to a transport reagent containing a polymer with comprising 6-25 subunits with a guanidino or amidino side chain moiety in at least 50% of the subunits.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for guanidinium compounds of formula (I).

m = 6 - 25;

- T =first terminal functional group or L (both optionally protected);
  - L = linking group having an attached therapeutic agent;
- W = second terminal functional group or L (both optionally protected);
  - Xi = backbone subunit;
  - i = numbering system of 1 25;
- Yi = H, amino acid side chain, (hetero)aryl, 1-8C alkylene, 2-8C alkenylene, 2-8C alkynylene, 2-8C heteroalkylene, 3-8C cycloalkylalkylene, 2-8C spirocycloalkylene and/or (hetero)arylene; n = 0 2;
- Zi = -NHC(=NH2)NH2(+), pyrrolidine-1-carboxamidin-yl, 2-amino-4,5-dihydro-3H-imidazol-1-ium-5-yl, imidazolidin-2-ylidene-ammonium-1-yl, 1,3-dihydro-benzoimidazol-2-ylidene-ammonium-1-yl, 1,3-dihydro-imidazol-2-ylidene-ammonium-1-yl, or 1,3-dihydro-benzoimidazol-2-ylidene-ammonium-yl; and provided that:
  - (i) when n is 0, then Yi is H, amino acid side chain, or

(hetero)arvl;

(ii) when n is 1, then Yi is 1-8C alkylene, 2-8C alkenylene, 2-8C alkynylene, 2-8C heteroalkylene, 3-8C cycloalkylalkylene, 2-8C spirocycloalkylene and/or (hetero)arylene;

(iii) T and W do not simultaneously contain an attached therapeutic agent; and

(iv) (I) has at least 4 quanidinium moieties and the position of the compound joining W and T is not a polypeptide.

USE - For enhancing transport of biological agents such as diagnostic agent, anticancer agent, antifungal agent, antibacterial agent or anti-inflammation agent, across a biological membrane (claimed). The method is also useful for screening the biological activity of agents which are unable or poorly able to enter cells by themselves.

ADVANTAGE - The method promotes transport of the conjugate across the membrane at a higher rate than the trans-membrane transport rate of the biological agent in the non-conjugated form. It provides an efficient way of identifying active agents that might not otherwise be accessible through large scale screening programs, for lack of an effective and convenient way of transporting the agent into the cell or organelle, and enables the testing of activities of agents that by themselves are unable or poorly able to enter cells to manifest biological activity. The delivery of small organic molecules having poor solubilities in aqueous liquids such as serum and aqueous saline can be administered in greater dosage and with more efficacy. Dwq.0/23

L15 ANSWER 10 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-229291 [22] WPIDS

2003-247851 [24] CROSS REFERENCE: · C2003-058853 DOC. NO. CPI:

TITLE: New colloidal carrier composition useful for e.g. passive

targeting of drugs to sites of pathology, comprises active agent and lipid-polymer conjugate comprising amphiphilic lipid and polymer e.g. poly-(amino acid

derivative). A23 A96 B07

DERWENT CLASS:

BRUIN, P; DE BOER, L W T; DE VRINGER, T; HENNINK, W E; INVENTOR(S):

METSELAAR, J M; OUSSOREN, C; STORM, G; DEBOER, L W T;

HENNICK, W E; THEODORUS, D B L W

PATENT ASSIGNEE(S): (YAMA) YAMANOUCHI EURO BV; (BRUI-I) BRUIN P; (DVRI-I) DE

> VRINGER T; (HENN-I) HENNICK W E; (METS-I) METSELAAR J M; (OUSS-I) OUSSOREN C; (STOR-I) STORM G; (THEO-I) THEODORUS

DBLW

COUNTRY COUNT: 91

PATENT INFORMATION:

KIND DATE PATENT NO WEEK LA PG -----

WO 2002098952 A1 20021212 (200322) \* EN 51

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AU BA BB BG BR BZ CA CN CO CR CU CZ DM DZ EC EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ OM PH

PL RO SG SI SK TT UA US UZ VN YU ZA

EP 1392755 A1 20040303 (200417) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

NO 2003005264 A 20040128 (200419)

SK 2003001597 A3 20040608 (200441) CZ 2003003480 A3 20040714 (200448)

KR 2004027512 A 20040401 (200451)

KR 2004027513 A 20040401 (200451)

| ΑU | 2002319248 | A1 | 20021216 | (200452) |    |    |
|----|------------|----|----------|----------|----|----|
| JP | 2004527586 | W  | 20040909 | (200459) |    | 84 |
| CN | 1520435    | Α  | 20040811 | (200476) |    |    |
| US | 2004241222 | A1 | 20041202 | (200480) |    |    |
| ZA | 2003008937 | Α  | 20050126 | (200513) |    | 57 |
| BR | 2002009699 | Α  | 20050201 | (200515) |    |    |
| IN | 2003001882 | P4 | 20041211 | (200530) | EN |    |
| MX | 2003011049 | A1 | 20040701 | (200545) |    |    |

# APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
| WO 2002098952 |      | WO 2002-EP6783 | 20020603 |
| EP 1392755    | A1   | EP 2002-748799 | 20020603 |
|               |      | WO 2002-EP6783 | 20020603 |
| NO 2003005264 | A    | WO 2002-EP6783 | 20020603 |
|               |      | NO 2003-5264   | 20031127 |
| SK 2003001597 | A3   | WO 2002-EP6783 | 20020603 |
|               |      | SK 2003-1597   | 20020603 |
| CZ 2003003480 | A3   | WO 2002-EP6783 | 20020603 |
|               |      | CZ 2003-3480   | 20020603 |
| KR 2004027512 | A    | KR 2003-715720 | 20031201 |
| KR 2004027513 | Α    | KR 2003-715722 | 20031201 |
| AU 2002319248 | A1   | AU 2002-319248 | 20020603 |
| JP 2004527586 | W    | WO 2002-EP6783 | 20020603 |
|               |      | JP 2003-502070 | 20020603 |
| CN 1520435    | Α    | CN 2002-812735 | 20020603 |
| US 2004241222 | A1   | WO 2002-EP6783 | 20020603 |
|               |      | US 2004-479031 | 20040617 |
| ZA 2003008937 | Α    | ZA 2003-8937   | 20031117 |
| BR 2002009699 | Α    | BR 2002-9699   | 20020603 |
|               |      | WO 2002-EP6783 | 20020603 |
| IN 2003001882 | P4   | WO 2002-EP6783 | 20020603 |
|               |      | IN 2003-CN1882 | 20031201 |
| MX 2003011049 | A1   | WO 2002-EP6783 | 20020603 |
|               |      | MX 2003-11049  | 20031201 |

## FILING DETAILS:

| PATENT NO  | KIND   | PATENT NO   |
|--|--|---|
| EP 1392755<br>SK 2003001597<br>CZ 2003003480<br>AU 2002319248<br>JP 2004527586 | Al Based on A3 Based on A3 Based on A1 Based on W Based on | WO 2002098952<br>WO 2002098952<br>WO 2002098952<br>WO 2002098952<br>WO 2002098952 |
| BR 2002009699<br>MX 2003011049   | A Based on<br>Al Based on                                  | WO 2002098952<br>WO 2002098952  |
|  |  |   |

PRIORITY APPLN. INFO: EP 2001-202107 20010601

AN 2003-229291 [22] WPIDS

CR 2003-247851 [24]

AB WO 200298952 A UPAB: 20050715

NOVELTY - New colloidal carrier composition (I) comprises: (i) an active agent; and

(ii) a lipid-polymer conjugate (Ia).
DETAILED DESCRIPTION - New colloidal carrier composition (I) comprises:

- (1) an active agent; and
- (2) a lipid-polymer conjugate (Ia) which is obtainable from amphiphilic lipid that consists of at least one hydrophobic apolar moiety

and hydrophilic polar **head** group, and polymer or its monomeric precursor, where the polymer is poly-(amino acid), poly-(amino acid derivative) or poly-(amino acid analog).

(Ia) provides long-circulating properties to (I).

ACTIVITY - Cytostatic; Antibacterial; Antiinflammatory.

USE - (I) is useful for providing a therapeutic agent, a biological agent, physiological agent, prophylactic or diagnostic agent (including imaging agents and radio-actively labeled compounds) in e.g. vesicular bilayer systems such as liposomes, niosomes and reversed vesicles, micellar systems, nanocapsules and nanospheres. (I) is also useful for passive targeting to sites of pathology (e.g. tumors, infection, inflammation) and for active targeting to cells in bloodstream, to endothelium. (I) is also useful as an artificial oxygen delivery system, blood-pool imaging and anti-fouling coating for biomaterials.

ADVANTAGE - The stability of liposomes prepared with (Ia) is improved as compared to that of conventional liposome preparations. (Ia) when incorporated into (I) provides long-circulating properties to these compositions. (Ia) is biodegradable and has reduced lipid-dose dependency as compared with polyethylene glycol-liposomes. An increased clearance after second injection of the composition is not always observed, and the reduction in blood circulation time is moderate. In an in vivo experimental arthritis model, one single intravenous injection of (I) appeared effective repeated injections of non-encapsulated corticosteroid compound or when encapsulated in conventional liposomes. Also, side effects associated with corticosteroid-based therapy will be reduced, due to reduction in the amount of corticosteroids that has to be administered.

DESCRIPTION OF DRAWING(S) - The figure shows a graphical representation of the mean values for the calculated percentage injected dose in blood samples versus time for polyethylene glycol-distearoyl phosphatidylethanolamine (PEG-DSPE)-containing liposomal preparations, having a different amount of lipid.

Dwg.1/6

L15 ANSWER 11 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-247851 [24] WPIDS

CROSS REFERENCE: 2003-229291 [22] DOC. NO. CPI: C2003-063721

TITLE: New lipid polymer conjugate useful for e.g. vesicular

bilayer systems for use e.g. in therapy,

comprises e.g. poly-amino acid derivative or poly-amino acid analogue polymer, and lipid attached to nitrogen or

carbon terminal of polymer.

DERWENT CLASS: A23 A96 B07

INVENTOR(S): BRUIN, P; DE BOER, L W T; DE VRINGER, T; HENNINK, W E; METSELAAR, J M; OUSSOREN, C; STORM, G; DE BRINGER, T;

METSELLAR, J M; DEBOER, L W T; HENNICK, W E; VRINGER, T D

PATENT ASSIGNEE(S): (YAMA) YAMANOUCHI EURO BV; (BRUI-I) BRUIN P; (DBOE-I) DE

BOER L W T; (HENN-I) HENNICK W E; (METS-I) METSELAAR J M; (OUSS-I) OUSSOREN C; (STOR-I) STORM G; (VRIN-I) VRINGER T

D

COUNTRY COUNT: 91

PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|-----------|------|------|------|----|----|
|           |      |      |      |    |    |

WO 2002098951 A2 20021212 (200324)\* EN 44

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AU BA BB BG BR BZ CA CN CO CR CU CZ DM DZ EC EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ OM PH

PL RO SG SI SK TT UA US UZ VN YU ZA

EP 1392756 A2 20040303 (200417) EN

## APPLICATION DETAILS:

MX 2003011050 A1 20040701 (200545)

| PATENT NO                   | KIND     | APPLICATION                      | DATE     |
|-----------------------------|----------|----------------------------------|----------|
| WO 2002098951<br>EP 1392756 | A2<br>A2 | WO 2002-EP6432<br>EP 2002-754661 | 20020603 |
| EF 1392/30                  | AZ       | WO 2002-734001                   | 20020603 |
| NO 2003005263               | А        | WO 2002-EP6432                   | 20020603 |
|                             |          | NO 2003-5263                     | 20031127 |
| SK 2003001598               | A3       | WO 2002-EP6432                   | 20020603 |
|                             |          | SK 2003-1598                     | 20020603 |
| CZ 2003003479               | A3       | WO 2002-EP6432                   | 20020603 |
|                             |          | CZ 2003-3479                     | 20020603 |
| AU 2002320851               | A1       | AU 2002-320851                   | 20020603 |
| JP 2004527585               | W        | WO 2002-EP6432                   | 20020603 |
|                             |          | JP 2003-502069                   | 20020603 |
| US 2004254352               | A1       | WO 2002-EP6432                   | 20020603 |
|                             |          | US 2004-479319                   | 20040723 |
| BR 2002009695               | Α        | BR 2002-9695                     | 20020603 |
|                             |          | WO 2002-EP6432                   | 20020603 |
| ZA 2003008938               | Α        | ZA 2003-8938                     | 20031117 |
| IN 2003001888               | P4       | WO 2002-EP6432                   | 20020603 |
|                             |          | IN 2003-CN1888                   | 20031201 |
| MX 2003011050               | A1       | WO 2002-EP6432                   | 20020603 |
|                             |          | MX 2003-11050                    | 20031201 |

# FILING DETAILS:

| KIND        | PATENT NO  |  |  |  |
|-------------|--|--|--|--|
| A2 Based on | WO 2002098951  |  |  |  |
| A3 Based on | WO 2002098951  |  |  |  |
| A3 Based on | WO 2002098951  |  |  |  |
| Al Based on | WO 2002098951  |  |  |  |
| W Based on  | WO 2002098951  |  |  |  |
| A Based on  | WO 2002098951  |  |  |  |
| Al Based on | WO 2002098951  |  |  |  |
|             | A2 Based on A3 Based on A3 Based on A1 Based on W Based on A Based on A Based on |  |  |  |

PRIORITY APPLN. INFO: EP 2001-202107 20010601

AN 2003-247851 [24] WPIDS

CR 2003-229291 [22]

AB WO 200298951 A UPAB: 20050715

NOVELTY - New lipid polymer **conjugate** (A) comprises at least one hydrophobic apolar moiety and a hydrophilic polar **head** group, and a polymer of specific formula or monomeric precursor having nitrogen (N) and carbon (C) terminal end groups.

The polymer is a poly-(amino acid), poly-(amino acid derivative) or a poly-(amino acid) analog.

The lipid is attached to N or C terminal of the polymer.

DETAILED DESCRIPTION - A lipid polymer conjugate comprises at least one hydrophobic apolar moiety and a hydrophilic polar head group, and a polymer of formula -(NHCHR(CH2)mCO)n- (I) or monomeric precursor having nitrogen (N) and carbon (C) terminal end groups.

The polymer is a poly-(amino acid), poly-(amino acid derivative) or a poly-(amino acid) analog.

The lipid is attached to N or C terminal of the polymer.

The lipid polymer is obtainable from an amphiphilic lipid.

R = H, -CH3, -CHCH3OR, -(CH2)xOR1, -(CH2)x-CO-NHR1, -(CH2)x-NH-CO-R1, -(CH2)x-SOyCH3, OR-(CH2)xCOOH;

R1 = hydrogen or 1-4C alkyl optionally substituted with one or more hydroxy groups or one di 1-4C alkylamine group;

x = 0-4;

m = 1 or 0; and

y = 1 or 2.

USE - (A) are used for inclusion into a colloidal carrier composition e.g. vesicular bilayer systems, such as liposomes, niosomes and reversed vesicles, micellar systems, nanocapsules and nanospheres and for use in therapy, diagnosis and prophylaxis.

ADVANTAGE - The polymer lipid conjugates (A) exhibits ability to reduce zeta potential, thus demonstrates the polymer grafting shielded the surface charge. The polymer lipid conjugates are biodegradable and hence provide no risk of accumulation in cells of animal or human body. (A) exhibits reduced lipid dose dependency. An increased clearance after second injection of the lipid polymer conjugate composition is not observed and the reduction in blood circulation time is moderate.

DESCRIPTION OF DRAWING(S) - The figure shows a graph showing the mean values for the calculated percentage injected dose in blood samples versus time for polyethylene glycol-poly(2-hydroxyethyl)-L-asparagine containing liposomal preparation having different amount of total lipid. Dwg.1/6

L15 ANSWER 13 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-434879 [46] WPIDS

DOC. NO. NON-CPI: N2002-342354 DOC. NO. CPI: C2002-123416

TITLE: Biocompatible material useful for e.g. controlling

cellular growth comprises at least two component surface.

DERWENT CLASS: A18 A23 A25 A96 B04 B07 D16 D22 P34

ALTANKOV, G; JANKOVA, K; JONSSON, G; THOM, V; ULBRICHT, M INVENTOR(S):

(SURF-N) SURFARC APS; (BIOS-N) BIOSURF APS; (ALTA-I) PATENT ASSIGNEE(S): ALTANKOV G; (JANK-I) JANKOVA K; (JONS-I) JONSSON G;

(THOM-I) THOM V; (ULBR-I) ULBRICHT M

COUNTRY COUNT: 98

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG \_\_\_\_\_\_

WO 2002015955 A2 20020228 (200246) \* EN 217

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO

RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

A 20020304 (200247) AU 2001081758

A2 20030716 (200347) EP 1326655 EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

US 2005053642 A1 20050310 (200519)

### APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
| WO 2002015955 | A2   | WO 2001-DK557  | 20010823 |
| AU 2001081758 | Α    | AU 2001-81758  | 20010823 |
| EP 1326655    | A2   | EP 2001-960202 | 20010823 |
|               |      | WO 2001-DK557  | 20010823 |
| US 2005053642 | A1   | WO 2001-DK557  | 20010823 |
|               |      | US 2003-362677 | 20030815 |

## FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               |             |               |
| AU 2001081758 | A Based on  | WO 2002015955 |
| EP 1326655    | A2 Based on | WO 2002015955 |

PRIORITY APPLN. INFO: DK 2000-1250 20000823

AN 2002-434879 [46] WPIDS

AB WO 200215955 A UPAB: 20040408

NOVELTY - Biocompatible material comprises a surface comprising at least two components such as a hydrophobic substratum and a macromolecule of hydrophobic nature.

DETAILED DESCRIPTION - Biocompatible material comprises a substratum (A) contacted by at least one macro-molecule. The material has a first advancing contact angle (a). (A) has a second advancing contacting angle b0 when not contacted by a macromolecule and another second advancing contact angle bsat, when the substratum is saturated by the macromolecules. The advancing contact angles are measured using water and air saturated by water vapor. The bsat does not change when the substratum is contacted by further macromolecules by a chemical bond. The relation between the advancing contact angles is R = (b0 - a)/(b0 - bsat) where R is 0 - less than 0.4.

INDEPENDENT CLAIMS are included for the following:

- (1) use of the material in the manufacture of an implantable organ or its part; and
  - (2) producing the material by:
- (i) contacting the substratum having a second contact angle with a composition comprising several macromolecules; and
- (ii) providing a biocompatible material comprising a substratum contacted by several macromolecules.

ACTIVITY - Antiinfertility.

MECHANISM OF ACTION - None given.

USE - For controlling cellular growth, cellular proliferation, and/or cellular differentiation; separating and/or isolating biological material; producing a biohybrid organ; diagnosis or carrying out therapy, carrying out surgery of human or animal or their parts; as a carrier for in vivo delivery of a medicament to a human or animal body (claimed); as cell culture dishes, bioreactors, implants, biohybrid organs e.g. pacemaker etc.; to create bio-compatible surfaces suitable for use in emerging technologies e.g. the construction and application of the surface architectures of biomaterials with innovative functionalities such as bioartificial pancreas, liver or kidney; to improve the implantation rates after in vitro fertilization; to treat and/or prevent infertility or early pregnancy loss; to provide a container capable of mimicking an endomaterial environment of a female uterus; to enhance fertility potential of animal oocytes e.g. sports, zoo, pet and farm animals; in a dialysis membrane; for making tissue engineered constructs, valves and vessels; to provide polymer-based drug release systems e.g. systems based on implantable materials; for bone reconstruction with tissue engineering vascularized bone; for engineering composite bone and

cartilage; to increase the mechanical strength and liability of e.g. heart valve leaflets and other engineered tissues; for growing vertebrate cells e.g. human cells including human skin cells; in skin grafting.

ADVANTAGE - (A) in cooperation with the macromolecule maintains, improves and/or stabilizes the biologically active form or its conformation. The biologically active compound improves contact between the material and a biological entity e.g. biological cell or virus or their parts, including a polypeptide or its part, nucleic acid, carbohydrate and/or lipid. The material does not induce an acute or chronic inflammatory response and does not prevent a proper differentiation of implant surrounding tissue. The method is simple and inexpensive. The surfaces can be used as cell culture dishes, bioreactors, implants etc. without the need of extensive development of new polymers and biocompatibility screening, ensures spatial separation of e.g. xenogenic and/or allogenic cells from the host immune system. The method increases the rate of maturation of immature oocytes and potential of fertilization of oocytes, minimizes incubation-time, and improves the quality of incubated oocytes. The degree of modification resulting from macromolecule including PEG attachment does not reduces the permeability of the membranes, thus suitable for the application as haemodialysis membrane. The tissue engineered constructs have improved mechanical strength and flexibility while retains biocompatible properties of the material. The valves and vessels withstand repeated stress and stirring. Dwg.0/31

L15 ANSWER 14 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-514501 [56] WPIDS

DOC. NO. CPI: C2001-153732

TITLE: Composition comprising a combination of an oxidizing

and/or reducing agent, a protein-denaturing agent, and a

hapten, useful for treating neoplasms, tumors, and

cancers.

DERWENT CLASS: B05 D16 INVENTOR(S): YU, B

PATENT ASSIGNEE(S): (YUBB-I) YU B

COUNTRY COUNT: 94

PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LA | PG |
|-----------|-----------|------|----|----|
|           |           |      |    |    |

WO 2001052868 A1 20010726 (200156)\* EN 83

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001030977 A 20010731 (200171) US 2002044919 A1 20020418 (200228)

CN 1431909 A 20030723 (200365)

JP 2004505009 W 20040219 (200414) 223

US 6811788 B2 20041102 (200472)

US 2005118187 A1 20050602 (200537)

# APPLICATION DETAILS:

| PATENT NO     | KIND           | APPLICATION     | DATE     |
|---------------|----------------|-----------------|----------|
| WO 2001052868 | A1             | WO 2001-US1737  | 20010118 |
| AU 2001030977 | A              | AU 2001-30977   | 20010118 |
| US 2002044919 | Al Provisional | US 2000-177024P | 20000119 |

|    |            |            |             | US | 2001-765060  | 20010117 |
|----|------------|------------|-------------|----|--------------|----------|
| CN | 1431909    | Α          |             | CN | 2001-806830  | 20010118 |
| JP | 2004505009 | W          |             | JP | 2001-552915  | 20010118 |
|    |            |            |             | WO | 2001-US1737  | 20010118 |
| US | 6811788    | В2         | Provisional | US | 2000-177024P | 20000119 |
|    |            |            |             | US | 2001-765060  | 20010117 |
| US | 2005118187 | <b>A</b> 1 | Provisional | US | 2000-177024P | 20000119 |
|    |            |            | CIP of      | US | 2001-765060  | 20010117 |
|    |            |            |             | US | 2004-973798  | 20041025 |

## FILING DETAILS:

AΒ

| PATENT NO                                       | KIND                                  | PATENT NO                                    |
|---|---------------------------------------|--|
| AU 2001030977<br>JP 2004505009<br>US 2005118187 | A Based on<br>W Based on<br>Al CIP of | WO 2001052868<br>WO 2001052868<br>US 6811788 |
| PRIORITY APPLN. INFO                            | : US 2000-177024P<br>2001-765060      | 20000119; US<br>20010117; US                 |

2004-973798

AN 2001-514501 [56] WPIDS

WO 200152868 A UPAB: 20011001

NOVELTY - A composition (I) comprising a combination of an oxidizing or reducing agent, a protein-denaturing agent, and a hapten, is new.

20041025

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- a kit comprising the combination (I);
- (2) an article of manufacture comprising:
- (a) packaging material;
- (b) the combination above; and
- (c) a label indicating that the article is for treating neoplasms; and
- (3) a method for treating neoplasm in a mammal comprising in situ administration to the neoplasm of a mammal, a hapten and a coagulation agent or treatment that causes coagulation of the neoplasm (an autologous immune response is generated against the neoplasm).

ACTIVITY - Cytostatic.

31 advanced stage IV liver cancer patients were treated using the new combination. Prior to procedure, patients were given a mild sedative or painkiller. Patients were calmed thoroughly and were also monitored by modern medial imaging. With local anesthesia, percutaneous puncture was administered directly into the tumor using a spinal needle connected to a high-power syringe containing a combination of ethanol, H2O2, anticancer drug AraC (8 mg/ml) and hemotoxilin (5 mg/ml). Combination was injected directly into the tumor and distributed throughout the matrix of the whole tumor. Sonic imaging showed the stranger echo imaging which indicated the coagulation area.

Following coagulation lysis and tumor cell death monitored by sonic imaging, which showed liquefied echo, tumor started to shrink and disappear. Normal tissues grew replacing the tumor. The process was monitored by medical imaging systems. The amount of the ingredients of the combination injected into the tumor was determined by the diameter of tumors (cm) with 2 ml of the combination for each centimeter.

Procedure was repeated in 1-2 weeks. On average, each patient was treated with the injection for 3 times. No severe side effects for all the treated patients was observed, although some patients experienced tolerable pain the injection site while a few had light fever during the first week. All side effects disappeared in about 1 week. No serious complications happened in any cases.

MECHANISM OF ACTION - Gene therapy.

USE - The combination and the methods are useful for treating

neoplasms, tumors, and cancers, including neoplasm or cancer of the e.g. adrenal gland, anus, auditory nerve, bile ducts, bladder, bone, brain, breast, bruccal, central nervous system, cervix, colon, ear, endometrium, esophagus, eye, eyelids, fallopian tube, gastrointestinal tract, head and neck, heart, kidney, larynx, liver, lung, or mandible.

The combination and methods may further be used in treating tumors of mesenchymal origin (e.g. connective tissue and derivatives, or endothelial and related tissues blood vessels), epithelial origin (stratified squamous carcinoma, or basal cells of skin or adenexa), and tumors derived from more than one neoplastic cell types derived from more than one germ layers.

The treatment may be used with radiation therapy, before surgery for the pre-treatment of neoplasm for easier removal of the neoplastic mass and reduces the neoplasm metastasis rate, or with gene therapy. Dwg. 0/4

L15 ANSWER 15 OF 38 MEDLINE on STN ACCESSION NUMBER: 2001673979 MEDLINE DOCUMENT NUMBER: PubMed ID: 11718771

Orienting otolith-ocular reflexes in the rabbit during TITLE:

static and dynamic tilts and off-vertical axis rotation.

Maruta J; Simpson J I; Raphan T; Cohen B AUTHOR:

Departments of Neurology and Physiology and Biophysics, CORPORATE SOURCE:

Mount Sinai School of Medicine, 1 East 100th Street, Box

1135, New York, NY 10029, USA.

Vision research, (2001) 41 (25-26) 3255-70. SOURCE:

Journal code: 0417402. ISSN: 0042-6989.

England: United Kingdom PUB. COUNTRY:

Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

English LANGUAGE:

Priority Journals; Space Life Sciences FILE SEGMENT:

ENTRY MONTH: 200203

ENTRY DATE: Entered STN: 20011126

Last Updated on STN: 20020413 Entered Medline: 20020311

Orienting otolith-ocular reflexes were assessed in rabbits using static AB tilt, off-vertical axis rotation (OVAR) and sinusoidal oscillation about earth-horizontal axes. In all paradigms, head pitch produced ocular counter-pitch and vergence, and head roll produced ocular counter-roll and conjugate yaw version. Thus, vergence and version are essential components of orienting reflexes along the naso-occipital and bitemporal axes. Vergence and version caused misalignment between the axes of eye and head movement during pitch and roll head movements. Semicircular canal input broadened the band-pass of these orienting reflexes, which would make them more appropriate when compensating for head movement during active motion.

L15 ANSWER 17 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2000-071650 [06] WPIDS

1996-393530 [39]; 1997-393702 [36]; 1998-145264 [13]; CROSS REFERENCE: 1998-457256 [39]; 1998-495982 [42]; 1999-204741 [17];

2000-147218 [13]; 2001-225814 [23]; 2002-089133 [12];

2002-105080 [14]

C2000-020448 DOC. NO. CPI:

Polymeric assay film for direct colorimetric detection of TITLE:

small molecules such as pathogens.

DERWENT CLASS: A89 B04 D16 J04

CHARYCH, D; NAGY, J; SPEVAK, W INVENTOR(S):

(REGC) UNIV CALIFORNIA PATENT ASSIGNEE(S): 1

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO  | KII | ND DATE | WEEK         | LA | PG |
|------------|-----|---------|--------------|----|----|
|            |     |         |              |    |    |
| US 6001556 | Δ   | 1999121 | 14 (200006)* | 2  | n  |

## APPLICATION DETAILS:

| PATENT NO  | KIND                          | APPLICATION  | DATE   |
|------------|-------------------------------|--|--|
| us 6001556 | A CIP of<br>CIP of<br>Cont of | US 1992-976697<br>US 1992-982189<br>US 1993-159927<br>US 1996-592724 | 19921113<br>19921125<br>19931130<br>19960126 |

PRIORITY APPLN. INFO: US 1993-159927 19931130; US 1992-976697 19921113; US 1992-982189 19921125; US 1996-592724 19960126

AN 2000-071650 [06] WPIDS

CR 1996-393530 [39]; 1997-393702 [36]; 1998-145264 [13]; 1998-457256 [39]; 1998-495982 [42]; 1999-204741 [17]; 2000-147218 [13]; 2001-225814 [23]; 2002-089133 [12]; 2002-105080 [14]

AB US 6001556 A UPAB: 20040928

NOVELTY - Polymeric assay films for direct colorimetric detection tests of small molecules, are new.

DETAILED DESCRIPTION - A polymerized **bilayer** film (I) comprises:

- (1) a conjugated polymer backbone (comprising a number of polymerized diacetylene monomers);
- (2) linker groups (which are covalently conjugated to the polymer backbone);
- (3) ligands (either sialic acid and/or carbohydrates with ordering heads groups covalently conjugated to the linker groups) with direct affinity for an analyte; and
  - (4) a support structure.

The ordering head groups are bound to the surface of the conjugated polymer backbone in positions not occupied by the linker groups. The polymerized bilayer film undergoes a detectable color change upon binding of the analyte to the ligands.

INDEPENDENT CLAIMS are also included for the following:

- (1) a method (II) of producing (I), comprising:
- (a) providing:
  - (i) ligands (carbohydrates) with a direct affinity for an analyte;
  - (ii) linker groups with 2 terminal ends;
  - (iii) lipid monomers;
  - (iv) lipid monomers comprising ordering head groups; and
  - (v) a support surface;
- (b) attaching the ligands to the lipid monomers so that the ligands are attached to one end of the linkers and the lipid monomers are attached to the other (to produce monomer-linear structural unit-ligand groups);
- (c) mixing the monomer-linear structural unit-ligand groups with lipid monomers comprising ordering heads;
- (d) spreading the mixture from step (c) on the support to form a bilayer film; and
- (e) polymerizing the bilayer film (to form the polymerized bilayer film (I)); and
- (2) a method for detecting an analyte, comprising contacting (I) with a sample thought to contain the analyte and detecting a color change in (I) (a color change is indicative of the presence of the analyte).
- USE (I) may be used for the direct detection of small molecules such as pathogens (e.g. influenza viruses, herpes virus, human immunodeficiency virus (HIV), coronavirus, encephalomyelitis, chlamydia,

rotavirus, polyomavirus, Streptococcus, Salmonella, sendai virus, mumps virus, Newcastle Disease virus, myxovirus, Escherichia coli, encephalomyocarditis virus and Plasmodium (claimed)). Other substances such as industrial materials, enzymes, hormones, cell wall fragments, blood components, disease indicators, cell components, antibodies, lectins and genetic material may also be detected using (I).

(I) also has application in feedstock and effluent monitoring, drug development and other types of medical testing.

ADVANTAGE - The use of (I) is easily automated, especially if a spectrometer is used to detect color changes. A multiple well system may be produced from (I) which allows inexpensive screening and sequential testing for analytes. (I) represents a new approach to the direct detection of a material using color changes in a monomolecular film which occurs when specifically bound to the target molecule. (I) is simple and inexpensive to produce.

(I) provides the advantages of both an immunoassay and chemical analysis in a single system. It has the inherent direct assay advantages of analytical chemistry methods and has a substantial environmental range of testing beyond that of immunoassays. This allows accommodation of various analytes in their most advantageous environmental parameters. Additionally, (I) allows rigorous direct analysis to occur even in very narrow environmental ranges, previously unavailable with analytical chemical techniques. The speed and simplicity of the color change indicator of (I) are its hallmark advantages.

Dwg.0/6

L15 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:243267 CAPLUS

DOCUMENT NUMBER: 131:15441

TITLE: Effect of PEG-lipid conjugates on the phase behavior

of phosphatidylethanolamine dispersions

AUTHOR(S): Koynova, R.; Tenchov, B.; Rapp, G.

CORPORATE SOURCE: Institute of Biophysics, Bulgarian Academy of

Sciences, Sofia, 1113, Bulg.

SOURCE: Colloids and Surfaces, A: Physicochemical and

Engineering Aspects (1999), 149(1-3), 571-575

CODEN: CPEAEH; ISSN: 0927-7757

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

The phase behavior of binary mixts. of hydrated dielaidoylphosphatidylethanolamine (DEPE) with two different PEG-lipid conjugates at a molar fraction below 0.2 has been studied by using time-resolved X-ray diffraction, and partial phase diagrams have been constructed. The studied conjugates comprise two saturated hydrocarbon acyl chains 14 carbon atoms long and PEG550 or PEG5000 chains covalently attached to a phosphoethanolamine polar head group, DMPE(PEG550) and DMPE(PEG5000), resp. When added in small amts. (10-20 mol%) to DEPE aqueous dispersions, both PEG-lipids favor the lamellar liquid crystalline (L $\alpha$ ) phase at the expense of the lamellar gel (L $\beta$ ) and the inverted hexagonal (HII) phases. One of the conjugates, DMPE(PEG550), shifts the L $\alpha$ -HII transition of DEPE to higher temps. by 2.5°C per mol% PEG-lipid, and induces the spontaneous formation of a cubic phase of space group Im3m in the DEPE dispersions. The cubic phase intrudes between the lamellar liquid crystalline and the inverted hexagonal

phases in the DEPE/DMPE(PEG550) phase diagram. Low amts. of the DMPE(PEG5000) conjugate only shift the L $\alpha$ -HII transition of DEPE to higher temps., at 5.2°C per mol% PEG-lipid, but does not promote the formation of addnl. phases. The resp. slopes for the L $\beta$ -L $\alpha$ , transition temperature depression are 10-15 times smaller. At > 15 mol% DMPE(PEG550) and at > 5 mol% DMPE(PEG5000), the non-lamellar

phases are eliminated from the phase diagrams. Structural data on the organization of the pure hydrated PEG-lipid conjugates are also provided, suggesting that these lipids form micelles and lamellae.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:471436 CAPLUS

DOCUMENT NUMBER: 129:78811

TITLE: Receptor membranes.

INVENTOR(S): Cornell, Bruce Andrew; Braach-maksvytis, Vijolrta

Lucija Brinislava

PATENT ASSIGNEE(S): Australian Membrane and Biotechnology Research

Institute, Australia

SOURCE: U.S., 14 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO.  | DATE       |
|------------------------|------|----------|------------------|------------|
|                        |      |          |                  |            |
| US 5766960             | Α    | 19980616 | US 1995-449895   | 19950523   |
| US 5436170             | Α    | 19950725 | US 1990-473932   | 19900125   |
| US 5693477             | Α    | 19971202 | US 1995-447569   | 19950523   |
| US 5741712             | Α    | 19980421 | US 1995-448178   | 19950523   |
| PRIORITY APPLN. INFO.: |      |          | AU 1987-3346 A   | 19870727   |
|                        |      |          | AU 1987-3348 A   | 19870727   |
|                        |      |          | AU 1987-3453 A   | 19870731   |
|                        |      |          | AU 1987-4478 A   | 19870921   |
|                        |      |          | US 1990-473932 A | . 19900125 |
|                        |      |          | WO 1988-AU273 W  | 19880727   |

A membrane comprising a closely packed array of self-assembling AΒ amphiphilic mols., and is characterized in that it incorporates a plurality of ion channels, and/or at least a proportion of the self-assembling mols. comprise a receptor mol. conjugated with a supporting entity. The ion channel is selected from the group consisting of peptides capable of forming helixes and aggregates thereof, coronands, cryptands, podands and combinations thereof. In the amphiphilic mols. comprising a receptor mol. conjugated with a supporting entity, the receptor mol. has a receptor site and is selected from the group consisting of Iqs, antibodies, antibody fragments, dyes, enzymes and lectins. "The supporting entity is selected from the group consisting of a lipid head group, a hydrocarbon chain(s), a cross-linkable mol. and a membrane protein. The supporting entity is attached to the receptor mol. at tan end remote from the receptor site. In preferred embodiments the ion channel is gramicidin A, and is preferable gated. Such membranes may be used in the formation of sensing devices.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 25 OF 38 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 93229518 MEDLINE DOCUMENT NUMBER: PubMed ID: 8471621

TITLE: Lipid-amphotericin B complex structure in solution: a

possible first step in the aggregation process in cell

membranes.

AUTHOR: Balakrishnan A R; Easwaran K R

CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science,

Bangalore.

SOURCE: Biochemistry, (1993 Apr 20) 32 (15) 4139-44.

Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199305

ENTRY DATE: Entered STN: 19930604

Last Updated on STN: 19930604 Entered Medline: 19930517

AB The interactions between the polyene antibiotic amphotericin B with dipalmitoylphosphatidylcholine were investigated in vesicles (using circular dichroism) and in chloroform solution (using circular dichroism and 1H, 13C, and 31P nuclear magnetic resonance). The results show that amphotericin B readily aggregates in vesicles and that the extent of aggregation depends on the lipid:drug concentration ratio. Introduction of sterol molecules into the membrane hastens the process of aggregation of amphotericin B. In chloroform solutions amphotericin B strongly interacts with phospholipid molecules to form a stoichiometric complex. The results suggest that there are interactions between the conjugated heptene stretch of amphotericin B and the methylene groups of lipid acyl chains, while the sugar moiety interacts with the phosphate head group by the formation of a hydrogen bond. A model is proposed for the lipid-amphotericin B complex, in which amphotericin B interacts equally well with the two lipid acyl chains, forming a 1:1 complex.

L15 ANSWER 27 OF 38 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 93123198 MEDLINE DOCUMENT NUMBER: PubMed ID: 1478927

TITLE: Induction of vesicle-to-micelle transition by bile salts

for DOPE vesicles incorporating immunoglobulin G.

AUTHOR: Lee E O; Kim J G; Kim J D

CORPORATE SOURCE: Department of Chemical Engineering and Bioprocess ERC,

Korea Advanced Institute of Science and Technology, Taejon.

SOURCE: Journal of biochemistry, (1992 Nov) 112 (5) 671-6.

Journal code: 0376600. ISSN: 0021-924X.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199302

ENTRY DATE: Entered STN: 19930226

Last Updated on STN: 19930226 Entered Medline: 19930208

AB The vesicle-to-micelle transition of immunoliposomes formed by dioleoylphosphatidyl-ethanolamine (DOPE) and palmitoyl-immunoglobulin G (p-IqG) was investigated in the presence of bile salts and conjugated bile salts. Turbidity and the release of calcein from liposomes were measured as a function of the amount of bile salts added and compared with the solubilizing profiles of the salts according to the number and configurational state of hydroxy groups in the cholate. The solubilizing phenomena by bile salts conjugated with glycine or taurine were investigated in comparison with non-conjugated bile salts. The solubilizing effect of bile salts on the bilayer of immunoliposomes increased remarkably with the number of hydroxy groups, but was not influenced by the configurational state of the hydroxy group. The half-maximal concentration of bile salts, defined as the concentration giving the half-maximum turbidity of liposome solutions, decreased with hydrophobicity in the phosphatidylcholine (PC) bilayer. The increase in the hydrophobicity of bile salts induces the ability to permeabilize and solubilize phospholipid vesicles. In the case of PC or PE liposome bilayers with inserted protein, bile salts conjugated with

taurine or glycine had lower hydrophobicity than non-conjugated bile salts and showed a lower half-maximal concentration. The conjugated bile salts are believed to interact with lipids and solubilize the bilayers, while the head groups of bile salts interact with the inserted protein and extract it from the lipid bilayer.

L15 ANSWER 28 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 1989-061259 [08] WPIDS

DOC. NO. NON-CPI: N1989-046623 DOC. NO. CPI: C1989-027144

TITLE: Receptor membrane for bio-sensors - comprising

a closely packed array of self-assembling amphiphilic molecules having ion channels and/or receptor molecules.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): BRAACH-MAKSVYTIS, V L B; CORNELL, B A; BRAACH-MAKSVYTIS,

V L; BRAACHMAKS, V L B; BRAACH-MAKSVYTIS, V

PATENT ASSIGNEE(S): (CSIR) COMMONWEALTH SCI & IND RES ORG; (AUME-N) AUSTRALIA

MEMBRANE & BIOTECHNOLOGY RES INST; (AUME-N) AUSTRALIAN

MEMBRANE & BIOTECHNOLOGY INST

COUNTRY COUNT: 15

PATENT INFORMATION:

| PAS | PENT NO      | KII | ND DATE  | WEEK         | LA PG |
|-----|--------------|-----|----------|--------------|-------|
| WO  | 8901159      | A   | 19890209 | (198908)* Ei | N 40  |
|     | RW: AT BE CH | DE  | FR GB IT | LI LU NL SE  |       |
|     | W: AU JP US  |     |          |              |       |
| ΑU  | 8821279      | Α   | 19890301 | (198923)     |       |
| EP  | 382736       | Α   | 19900822 | (199034)     |       |
|     | R: AT BE CH  | DE  | FR GB IT | LI LU NL SE  |       |
| JP  | 03503209     | W   | 19910718 | (199135)     |       |
| ΕP  | 382736       | В1  | 19941102 | (199442) E   | 1 24  |
|     | R: AT BE CH  | DE  | FR GB IT | LI LU NL SE  |       |
| DE  | 3852036      | G   | 19941208 | (199503)     |       |
|     | 382736       |     |          |              |       |
| CA  | 1335879      |     |          |              |       |
| US  |              |     |          | (199535)     | 15    |
|     | 2682859      | B2  | 19971126 | (199801)     | 14    |
|     | 5693477      |     |          |              | 13    |
| US  | 5741712      | Α   |          |              | 13    |
| US  | 5766960      | Α   | 19980616 | (199831)     |       |

### APPLICATION DETAILS:

| PATENT NO   | KIND      | APPLICATION     | DATE     |
|-------------|-----------|-----------------|----------|
| WO 8901159  | Α         | WO 1988-AU273   | 19880727 |
| EP 382736   | Α         | EP 1988-907164  | 19880727 |
| JP 03503209 | W         | JP 1988-506329  | 19880727 |
| EP 382736   | B1        | EP 1988-907164  | 19880727 |
|             |           | WO 1988-AU273   | 19880727 |
| DE 3852036  | G         | DE 1988-3852036 | 19880727 |
|             |           | EP 1988-907164  | 19880727 |
|             |           | WO 1988-AU273   | 19880727 |
| EP 382736   | A4        | EP 1988-907164  |          |
| CA 1335879  | C         | CA 1988-573217  | 19880727 |
| US 5436170  | A         | WO 1988-AU273   | 19880727 |
|             |           | US 1990-473932  | 19900125 |
| JP 2682859  | B2        | JP 1988-506329  | 19880727 |
|             |           | WO 1988-AU273   | 19880727 |
| US 5693477  | A Cont of | US 1990-473932  | 19900125 |
|             |           | US 1995-447569  | 19950523 |

| US 5741712 | Α | Div ex | US | 1990-473932 | 19900125 |
|------------|---|--------|----|-------------|----------|
|            |   |        | US | 1995-448178 | 19950523 |
| US 5766960 | Α | CIP of | US | 1990-473932 | 19900125 |
|            |   |        | US | 1995-449895 | 19950523 |

### FILING DETAILS:

| PATENT NO   | KIND               | PATENT NO    |
|-------------|--------------------|--------------|
| EP 382736   | Bl Based on        | WO 8901159   |
| DE 3852036  | G Based on         | · EP 382736  |
|             | Based on           | WO 8901159   |
| US 5436170  | A Based on         | WO 8901159   |
| JP 2682859  | B2 Previous Publ.  | JP 03503209  |
|             | Based on           | WO 8901159   |
| US 5693477  | A Cont of          | US 5436170   |
| US 5741712  | A Div ex           | US 5436170   |
| US 5766960  | A CIP of           | US 5436170   |
| RITY APPLN. | INFO: AU 1987-4478 | 19870921; AU |

PRIORITY APPLN. INFO: AU 1987-4478 19870921; AU 1987-3346 19870727; AU 1987-3348 19870727; AU 1988-21279 19870728; AU 1987-3453 19870731

AN 1989-061259 [08] WPIDS

AB WO 8901159 A UPAB: 19960520

A membrane comprising a closely packed array of self-assembling amphiphilic molecules is claimed characterised in that (1) the membrane includes ion channels selected from peptides capable of forming helices and aggregates, podands, coronands, cryptands and combinations and/or (2) at least a proportion of the self-assembling amphiphilic molecules comprise a receptor molecule conjugated with a supporting entity, the receptor molecule having a receptor site and being selected from immunoglobulins, antibodies, antibody fragments, dyes, enzymes and lectins, the supporting entity being selected from a lipid head gp., a hydrocarbon chain, a cross-linkable molecule and a membrane protein, the supporting entity being conjugated with the receptor molecule at an end remote from the receptor site.

Pref. the ion channels are gramicidin or analogues. Also claimed is a biosensor comprising a membrane bilayer attached to a solid surface, the bilayer having an upper and lower layer, the lower layer being adjacent the solid surface and being provided with gps. reactive with the solid surface or with gps. provided on this, each layer of the bilayer being composed of self-assembling amphiphilic molecules and gramicidin monomers, and where a receptor moiety is attached to the gramicidin monomers in the upper layer. The solid surface is pref. a palladium-coated glass electrode.

USE/ADVANTAGE - The membranes are used partic. for the production of biosensors. They have a high density of receptor sites and serve as highly selective binding surfaces to which molecular species to be detected will bind.

0/6

Dwg.0/6

ABEQ EP 382736 B UPAB: 19941212

A membrane bound to a solid non-porous surface, the membrane comprising a closely packed array of self-assembling amphiphillic molecules and characterised in that:

- (1) the membrane includes a plurality of ion channels which are peptides capable of forming helices and aggregates thereof, a podand, coronand, cryptand or a combination thereof; and
- (2) at least a proportion of the self-assembling amphiphillic molecules comprise a receptor molecule conjugated with a supporting

entity, the receptor molecule having a receptor site and being an immunoglobulin, antibody, antibody fragment, dye, enzyme or lectin;

the supporting entity being a lipid head group, a hydrocarbon chain(s), a cross-linkable molecule or a membrane protein and being conjugated with the receptor molecule at an end remote from the receptor site.

Dwg.0/6

ABEQ US 5436170 A UPAB: 19950905

Membrane comprises a closely packed array of self-assembling amphiphilic molecules, e.g. peptides that form helices and/or aggregates, such that numerous ion channels are present in the structure and at least part of the structure comprises a receptor (e.g. immunoglobulin, antibody or its active binding fragment, enzyme or lectin) conjugated with a hydrocarbon chain or membrane protein at a location remote from the receptor's active site.

USE - The prods. are components of selective biosensors. ADVANTAGE - The **membrane** is mounted on a solid supporting surface to provide robustness and avoid fragility. Dwg.0/6

ABEQ US 5693477 A UPAB: 19980119

A membrane comprising a closely packed array of self-assembling amphiphilic molecules is claimed characterised in that (1) the membrane includes ion channels selected from peptides capable of forming helices and aggregates, podands, coronands, cryptands and combinations and/or (2) at least a proportion of the self-assembling amphiphilic molecules comprise a receptor molecule conjugated with a supporting entity, the receptor molecule having a receptor site and being selected from immunoglobulins, antibodies, antibody fragments, dyes, enzymes and lectins, the supporting entity being selected from a lipid head gp., a hydrocarbon chain, a cross-linkable molecule and a membrane protein, the supporting entity being conjugated with the receptor molecule at an end remote from the receptor site.

Pref. the ion channels are gramicidin or analogues. Also claimed is a biosensor comprising a membrane bilayer attached to a solid surface, the bilayer having an upper and lower layer, the lower layer being adjacent the solid surface and being provided with gps. reactive with the solid surface or with gps. provided on this, each layer of the bilayer being composed of self-assembling amphiphilic molecules and gramicidin monomers, and where a receptor moiety is attached to the gramicidin monomers in the upper layer. The solid surface is pref. a palladium-coated glass electrode.

USE/ADVANTAGE - The membranes are used partic. for the prodn. of biosensors. They have a high density of receptor sites and serve as highly selective binding surfaces to which molecular species to be detected will bind.

Dwg.3/6

L15 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:109884 CAPLUS

DOCUMENT NUMBER: 108:109884

TITLE: Differential localization of glycoconjugates having

affinity for concanavalin A on the surface of the sperm head in the testis, the epididymis, and the

ejaculate of the ram

AUTHOR(S): Delpech, S.; Hamamah, S.; Pisselet, C.; Courot, M.

CORPORATE SOURCE: INRA, Nouzilly, 37380, Fr.

SOURCE: Journal of Experimental Zoology (1988), 245(1), 59-62

CODEN: JEZOAO; ISSN: 0022-104X

DOCUMENT TYPE: Journal LANGUAGE: English

AB The location of Con A receptors on the surface of the head of ram spermatozoa originating from the rete testis, from 3 regions of the

epididymis, or from the ejaculate was investigated by using a Au-Con A labeling technique. Electron microscopic observation revealed 3 major localizations, each being characteristic of the origin of the spermatozoa: periacrosomal in the rete testis, postacrosomal in the epididymis, on the entire surface of the sperm head in the ejaculate.

L15 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1987:419734 CAPLUS

DOCUMENT NUMBER: 107:19734

TITLE: pH-dependent stability and fusion of liposomes

combining protonatable double-chain amphiphiles with

phosphatidylethanolamine

AUTHOR(S): Leventis, Rania; Diacovo, Thomas; Silvius, John R. CORPORATE SOURCE: Dep. Biochem., McGill Univ., Montreal, QC, H3G 1Y6,

Can.

SOURCE: Biochemistry (1987), 26(12), 3267-76

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal LANGUAGE: English

AB A series of novel double-chain amphiphiles with protonatable head groups were prepared including acylated derivs. of various 2-substituted palmitic acids, amino acid conjugates of these species, and

1,2-dioleoyl-3-succinylglycerol. These species can be combined with phosphatidylethanolamine (PE) to prepare reverse-phase evaporation vesicles

that

are stable and trap hydrophilic solutes at pH 7. At weakly acidic pH values (≤6.5, depending on the titratable amphiphilic component), these pH-sensitive vesicles exhibit fusion, with a limited extent of contents mixing and extensive mixing of lipids, accompanied by leakage of aqueous contents. Protons and divalent cations show strong synergistic effects in promoting mixing of both lipids and aqueous contents between pH-sensitive vesicles prepared with any of a variety of double-chain titratable amphiphiles. Calorimetric results indicate that the relative stabilities of different types of pH-sensitive liposomes at low pH cannot be simply correlated with the propensity of the lipids to form a hexagonal II phase under these conditions. Fluorescence measurements demonstrate that single-chain fatty acids, but not double-chain titratable amphiphiles such as N-acyl-2-aminopalmitic acids, are rapidly removed from pH-sensitive vesicles in the presence of other lipid vesicles, serum albumin, or serum. Addnl., pH-sensitive liposomes containing double-chain titratable amphiphiles retain their aqueous contents better than do those containing single-chain amphiphiles in the presence of lipid membranes or albumin. Surprisingly, however, pH-sensitive vesicles of either type show retention of contents in the presence of serum that is comparable to that observed with vesicles composed purely of phospholipids. A model is proposed to explain these latter findings.

L15 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1986:84801 CAPLUS

DOCUMENT NUMBER: 104:84801

TITLE: Identifying regions of membrane proteins in contact with phospholipid head groups: covalent

attachment of a new class of aldehyde lipid labels to

cytochrome c oxidase

AUTHOR(S): McMillen, Debra A.; Volwerk, Johannes J.; Ohishi,

Junichi; Erion, Mark; Keana, John F. W.; Jost,

Patricia C.; Griffith, O. Hayes

CORPORATE SOURCE: Inst. Mol. Biol., Univ. Oregon, Eugene, OR, 97403, USA

SOURCE: Biochemistry (1986), 25(1), 182-93

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE: Journal LANGUAGE: English

A series of amine-specific reagents based on the benzaldehyde reactive group have been synthesized, characterized, and used to study beef heart cytochrome c oxidase reconstituted in phospholipid bilayers. The series contained 3 classes of reagents, lipid-soluble phosphodiesters having a single hydrocarbon chain, phospholipid analogs, and a water-soluble benzaldehyde. All reagents were either radiolabeled or spin-labeled or both. The Schiff bases formed by these benzaldehydes with amines were reversible until the addition of the reducing agent Na cyanoborohydride, whereas attachment of lipid-derived aliphatic aldehydes was not readily reversible in the absence of the reducing agent. The benzaldehyde group provides a convenient method of controlling and delaying permanent attachment to integral membrane proteins until after the reconstitution steps. This ensures that the lipid analogs are located properly to identify amine groups at the lipid-protein interface rather than reacting indiscriminately with amines of the hydrophilic domains of the protein. The benzaldehyde lipid labels attached to cytochrome c oxidase with high efficiency. Typically, 20% of the amount of lipid label present was covalently attached to the protein, and the number of moles of label incorporated per mol of protein ranged 1-6, depending on the molar ratios of label, lipid, and protein. The efficiency of labeling by the water-soluble benzaldehyde was much less than that observed for any of the lipid

labels because of dilution effects, but equivalent levels of incorporation were achieved by increasing the label concentration ESR spectra of a nitroxide-containing

phospholipid analog covalently attached to reconstituted cytochrome c oxidase exhibited a large motion-restricted component, which is characteristic of spin-labeled lipids in contact with the hydrophobic surfaces of membrane proteins. The line shape and splittings were similar for covalently attached label and label free to diffuse and contact the protein mols. in the bilayer, providing independent evidence that the coupling occurs at the protein-lipid interface. The distribution of the benzaldehyde reagents attached to the polypeptide components of cytochrome c oxidase was examined by SDS polyacrylamide gel electrophoresis. The labeling pattern observed for the lipid analogs was not affected by the presence of the nitroxide moiety on the acyl chains but was dependent on the molar ratio of labeling reagent to protein. With the lipid labels, band VII was the most heavily labeled, and significant labeling of bands III, V, and VI was observed at higher labeling ratios. There was little or no labeling of bands I, II, and IV. A different labeling pattern was observed with the water-soluble label, providing addnl. evidence that the lipid-like benzaldehyde reagents react with cytochrome c oxidase from the confines of the bilayer. Thus, these new labels have the necessary specificity and reactivity to be useful in correlating sequence data with the structure and function of integral membrane proteins, particularly in identifying regions in contact with phospholipid head groups at the lamellar interface.

L15 ANSWER 36 OF 38 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 82182979 MEDLINE DOCUMENT NUMBER: PubMed ID: 6176271

TITLE: A novel approach for the topographical localization of

glycolipids on the cell surface.

AUTHOR: Spiegel S; Skutelsky E; Bayer E A; Wilchek M

CONTRACT NUMBER: F32-ES5120 (NIEHS)

SOURCE: Biochimica et biophysica acta, (1982 Apr 23) 687 (1) 27-34.

Journal code: 0217513. ISSN: 0006-3002.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198207

ENTRY DATE:

Entered STN: 19900317

Last Updated on STN: 19970203 Entered Medline: 19820719

In this study we have developed a prototype system for distinguishing AB between the topographical distribution of glycolipids versus glycoproteins on the ultrastructural level. Direct modification of membrane -based sialic acids with biotin groups labels both glycolipids and glycoproteins. In this case, subsequent ultrastructural localization of biotinylated sites would not discern between these two classes of glycoconjugate in an unambiguous manner. When biotinylated cells are fixed prior to interaction with ferritin-conjugated avidin, the mean distance of marker molecules from the membrane bilayer is 8.0 nm. In contrast, if the cells are allowed to cap through the action of ferritin-avidin conjugates on unfixed cells, the average distance (13.0 nm) of the marker molecules appears even more distant from the membrane on the capped portion of the cell (uropod), whereas those on the head region are positioned in close proximity to the bilayer (3.7 nm). In order to exclusively label cell surface glycolipids on the ultrastructural level, bovine brain gangliosides were biotinylated in vitro and the haptenized gangliosides were incorporated into intact cells. In this case, marker molecules denoting the incorporated gangliosides were found in relatively close juxtaposition to the membrane surface, in a manner strikingly similar to the labeling pattern of the head region on capped cells. These results support the concept that, in the native state, the carbohydrate portion of glycolipids is positioned closer to the membrane bilayer than that of glycoproteins.

=> (cap or capping) and membrane and antibod? 2107 (CAP OR CAPPING) AND MEMBRANE AND ANTIBOD? => py>1999<-----SEARCH ENDED BY USER => ≃> => py>1999 and 116 305 PY>1999 AND L16 => 116 not 117 1802 L16 NOT L17 => py>1998 and 118 63 PY>1998 AND L18 => 118 not 119 1739 L18 NOT L19 => t ti 120 1-50 L20 ANSWER 1 OF 1739 MEDLINE on STN Immunolocalization of integrin-like proteins in Arabidopsis and Chara. L20 ANSWER 2 OF 1739 MEDLINE on STN Mechanotransduction molecules in the plant gravisensory response: amyloplast/statolith membranes contain a beta 1 integrin-like protein.

- L20 ANSWER 3 OF 1739 MEDLINE on STN
- TI Central root cap cells are depleted of endoplasmic microtubules and actin microfilament bundles: implications for their role as gravity-sensing statocytes.
- L20 ANSWER 4 OF 1739 MEDLINE on STN
- TI Microsomal membrane proteins and vanadate-sensitive ATPase from Vicia faba root tips after clinostat treatment.
- L20 ANSWER 5 OF 1739 MEDLINE on STN
- TI Purification and immunolocalization of an annexin-like protein in pea seedlings.
- L20 ANSWER 6 OF 1739 MEDLINE on STN
- TI Developmental regulation of lymphocyte-specific protein 1 (LSP1) expression in thymus during human T-cell maturation.
- L20 ANSWER 7 OF 1739 MEDLINE on STN
- TI Odontoblast differentiation: a response to environmental calcium?.
- L20 ANSWER 8 OF 1739 MEDLINE on STN
- TI Gamma-glutamyl transpeptidase, an ecto-enzyme regulator of intracellular redox potential, is a component of TM4 signal transduction complexes.
- L20 ANSWER 9 OF 1739 MEDLINE on STN
- TI An analysis of microvessel density, androgen receptor, p53 and HER-2/neu expression and Gleason score in prostate cancer . preliminary results and therapeutic implications.
- L20 ANSWER 10 OF 1739 MEDLINE on STN
- TI Human cementum tumor cells have different features from human osteoblastic cells in vitro.
- L20 ANSWER 11 OF 1739 MEDLINE on STN
- TI The effects of brefeldin A on acrosome formation and protein transport to the acrosome in organ cultures of rat seminiferous tubules.
- L20 ANSWER 12 OF 1739 MEDLINE on STN
- TI A novel dipstick developed for rapid Bet v 1-specific IgE detection: recombinant allergen immobilized via a monoclonal **antibody** to crystalline bacterial cell-surface layers.
- L20 ANSWER 13 OF 1739 MEDLINE on STN
- TI Adducin is an in vivo substrate for protein kinase C: phosphorylation in the MARCKS-related domain inhibits activity in promoting spectrin-actin complexes and occurs in many cells, including dendritic spines of neurons.
- L20 ANSWER 14 OF 1739 MEDLINE on STN
- TI Heterogeneity in the presence of CD4-like molecules on human spermatozoa.
- L20 ANSWER 15 OF 1739 MEDLINE on STN
- TI Virulence and functions of myosin II are inhibited by overexpression of light meromyosin in Entamoeba histolytica.
- L20 ANSWER 16 OF 1739 MEDLINE on STN
- TI Radiation-induced apoptosis in human lymphocytes and lymphoma cells critically relies on the up-regulation of CD95/Fas/APO-1 ligand.
- L20 ANSWER 17 OF 1739 MEDLINE on STN
- TI Peripheral blood lymphocytes from psoriatic patients are hyporesponsive to beta-streptococcal superantigens.

- L20 ANSWER 18 OF 1739 MEDLINE on STN
- TI An essential role for the interaction between hyaluronan and hyaluronan binding proteins during joint development.
- L20 ANSWER 19 OF 1739 MEDLINE on STN
- TI The olfactory adenylyl cyclase III is expressed in rat germ cells during spermiogenesis.
- L20 ANSWER 20 OF 1739 MEDLINE on STN
- TI Downregulation of the beta4 integrin subunit in prostatic carcinoma and prostatic intraepithelial neoplasia.
- L20 ANSWER 21 OF 1739 MEDLINE on STN
- TI Molecular cloning and characterization of P47, a novel boar sperm-associated zona pellucida-binding protein homologous to a family of mammalian secretory proteins.
- L20 ANSWER 22 OF 1739 MEDLINE on STN
- TI Association of an 80 kDa protein with C-CAM1 cytoplasmic domain correlates with C-CAM1-mediated growth inhibition.
- L20 ANSWER 23 OF 1739 MEDLINE on STN
- TI Colon carcinoma cells use different mechanisms to escape CD95-mediated apoptosis.
- L20 ANSWER 24 OF 1739 MEDLINE on STN
- TI A crossreactivity at the immunoglobulin E level of the cell wall mannoproteins of Candida albicans with other pathogenic Candida and airborne yeast species.
- L20 ANSWER 25 OF 1739 MEDLINE on STN
- TI Simultaneous quantitation of specific IgE against 20 purified allergens in allergic patients sera by checkerboard immunoblotting (CBIB).
- L20 ANSWER 26 OF 1739 MEDLINE on STN
- TI Binding of the soluble, truncated form of an Fc receptor (mouse Fc gamma RII) to membrane-bound IgG as measured by total internal reflection fluorescence microscopy.
- L20 ANSWER 27 OF 1739 MEDLINE on STN
- TI Antibody-induced and cytoskeleton-mediated redistribution and shedding of viral glycoproteins, expressed on pseudorabies virus-infected cells.
- L20 ANSWER 28 OF 1739 MEDLINE on STN
- TI Superantigenicity of helper T-cell mitogen (SPM-2) isolated from culture supernatants of Streptococcus pyogenes.
- L20 ANSWER 29 OF 1739 MEDLINE on STN
- TI Costimulatory molecules in human atherosclerotic plaques: an indication of antigen specific T lymphocyte activation.
- L20 ANSWER 30 OF 1739 MEDLINE on STN
- TI Epstein-Barr virus-encoded LMP-1 protein upregulates the pNDCF group of nucleoskeleton-cytoskeleton-associated proteins.
- L20 ANSWER 31 OF 1739 MEDLINE on STN
- TI Visualization of Golgi apparatus in methacrylate embedded conifer embryo tissue using the monoclonal **antibody** JIM 84.
- L20 ANSWER 32 OF 1739 MEDLINE on STN
- TI Leukosialin (CD43, sialophorin) redistribution in uropods of polarized

neutrophils is induced by CD43 cross-linking by antibodies, by colchicine or by chemotactic peptides.

- L20 ANSWER 33 OF 1739 MEDLINE on STN
- TI Localization of nerve cells in the developing rat tooth.
- L20 ANSWER 34 OF 1739 MEDLINE on STN
- TI Immunohistochemical localization of nerve fibres during development of embryonic rat molar using peripherin and protein gene product 9.5 antibodies.
- L20 ANSWER 35 OF 1739 MEDLINE on STN
- TI The antigen receptor complex on cord B lymphocytes.
- L20 ANSWER 36 OF 1739 MEDLINE on STN
- TI Identification of two regions in the N-terminal domain of ActA involved in the actin comet tail formation by Listeria monocytogenes.
- L20 ANSWER 37 OF 1739 MEDLINE on STN
- TI Nitric oxide inhibits capping in HL-60 cells.
- L20 ANSWER 38 OF 1739 MEDLINE on STN
- TI Fibrin(ogen) and von Willebrand factor deposition are associated with intimal thickening after balloon angioplasty of the rabbit carotid artery.
- L20 ANSWER 39 OF 1739 MEDLINE on STN
- TI Markers of bone and cementum formation accumulate in tissues regenerated in periodontal defects treated with expanded polytetrafluoroethylene membranes.
- L20 ANSWER 40 OF 1739 MEDLINE on STN
- TI Local accumulation of alpha-spectrin-related protein under plasma membrane during capping and phagocytosis in Acanthamoeba.
- L20 ANSWER 41 OF 1739 MEDLINE on STN
- TI Effects of Ajoene on lymphocyte and macrophage membrane -dependent functions.
- L20 ANSWER 42 OF 1739 MEDLINE on STN
- TI An Aplysia cell adhesion molecule associated with site-directed actin filament assembly in neuronal growth cones.
- L20 ANSWER 43 OF 1739 MEDLINE on STN
- TI Analysis of yeast trimethylguanosine-capped RNAs by midwestern blotting.
- L20 ANSWER 44 OF 1739 MEDLINE on STN
- TI Cell adhesion molecules NgCAM and axonin-1 form heterodimers in the neuronal membrane and cooperate in neurite outgrowth promotion.
- L20 ANSWER 45 OF 1739 MEDLINE on STN
- TI CD66: role in the regulation of neutrophil effector function.
- L20 ANSWER 46 OF 1739 MEDLINE on STN
- TI Presence of the elastin-laminin receptor on human activated lymphocytes.
- L20 ANSWER 47 OF 1739 MEDLINE on STN
- TI ANCA defines the clinical disease manifestations of vasculitis.
- L20 ANSWER 48 OF 1739 MEDLINE on STN
- TI Association of murine splenocyte CD3 complex to the cytoskeleton: absence of modulation by exogenous fatty acids.

L20 ANSWER 49 OF 1739 MEDLINE on STN

Association of the tetraspan protein CD9 with integrins on the surface of S-16 Schwann cells.

L20 ANSWER 50 OF 1739 MEDLINE on STN

Evidence for the presence of immunoglobulin E antibodies specific to the cell wall phosphomannoproteins of Candida albicans in patients with allergies.

=> d ibib abs 120 27,32,44,50

L20 ANSWER 27 OF 1739 MEDLINE on STN ACCESSION NUMBER: 1998001342 MEDLINE DOCUMENT NUMBER: PubMed ID: 9343177

Antibody-induced and cytoskeleton-mediated TITLE:

redistribution and shedding of viral glycoproteins,

expressed on pseudorabies virus-infected cells.

Favoreel H W; Nauwynck H J; Van Oostveldt P; Mettenleiter T AUTHOR:

C; Pensaert M B

Laboratory of Virology, Faculty of Veterinary Medicine, CORPORATE SOURCE:

University of Ghent, Belgium.

Journal of virology, (1997 Nov) 71 (11) 8254-61. SOURCE:

Journal code: 0113724. ISSN: 0022-538X.

United States PUB. COUNTRY:

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199711

ENTRY DATE: Entered STN: 19971224

> Last Updated on STN: 19971224 Entered Medline: 19971113

AB Fluorescein isothiocyanate-labeled porcine pseudorabies virus (PrV) polyclonal antibodies were added to PrV-infected swine kidney cells in vitro at 37 degrees C. In approximately 47% of the infected cells, the addition induced passive patching and subsequent energy- and microtubule-dependent capping of all viral envelope glycoproteins, expressed on the plasma membranes of the infected cells. Further contraction and extrusion of the capped viral glycoproteins occurred in approximately 30% of the capped cells 2 h after the addition of antibodies and was accompanied by a concentration of F-actin beneath the caps. At that time, about 18% of the extruded caps were shed spontaneously into the surrounding medium. Mechanical force released 85% of the extruded caps, leaving viable cells with no microscopically detectable levels of viral glycoproteins on their plasma membranes. Experiments with PrV deletion mutants showed that viral glycoproteins gE and gI are important in triggering viral glycoprotein redistribution. Since the PrV gE-gI complex exhibits Fc receptor activity which facilitates capping, the importance of gE and gI may be partially explained by antibody bipolar bridging.

L20 ANSWER 32 OF 1739 MEDLINE on STN ACCESSION NUMBER: 97367997 MEDLINE DOCUMENT NUMBER: PubMed ID: 9224764

TITLE: Leukosialin (CD43, sialophorin) redistribution in uropods

of polarized neutrophils is induced by CD43 cross-linking

by antibodies, by colchicine or by chemotactic

peptides.

AUTHOR: Seveau S; Lopez S; Lesavre P; Guichard J; Cramer E M;

Halbwachs-Mecarelli L

CORPORATE SOURCE: INSERM U90 Hopital Necker, Paris, France. SOURCE: Journal of cell science, (1997 Jul) 110 ( Pt 13) 1465-75.

Journal code: 0052457. ISSN: 0021-9533.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199709

ENTRY DATE: Entered STN: 19971008

Last Updated on STN: 19971008 Entered Medline: 19970922

AB We investigated a possible association of leukosialin (CD43), the major surface sialoglycoprotein of leukocytes, with neutrophil cytoskeleton. We first analysed the solubility of CD43 in Triton X-100 and observed that CD43 of resting neutrophils was mostly soluble. The small proportion of CD43 molecules, which 'spontaneously' precipitated in Triton, appeared associated with F-actin, as demonstrated by the fact that this insolubility did not occur when cells were incubated with cytochalasin B or when F-actin was depolymerized with DNase I in the Triton precipitate. Cell stimulation with anti-CD43 mAb (MEM59) enhanced this CD43-cytoskeleton association. By immunofluorescence as well as by electron microscopy, we observed a redistribution of CD43 on the neutrophil membrane, initially in patches followed by caps, during anti-CD43 cross-linking at 37 degrees C. This capping did not occur at 4 degrees C and was inhibited by cytochalasin B and by a myosin disrupting drug butanedione monoxime, thus providing evidence that the actomyosin contracile sytem is involved in the capping and further suggesting an association of CD43 with the cytoskeleton. the capped cells exhibited a front-tail polarization with CD43 caps located in the uropod at the rear of the cell. Surprisingly, colchicine and the chemotactic factor fNLPNTL which induce neutrophil polarization associated with cell motility, also resulted in a clustering of CD43 in the uropod, independently of a cross-linking of the molecule by mAbs. An intracellular redistribution of F-actin, mainly at the leading front and of myosin in the tail, was observed during CD43 clustering induced by colchicine and in cells polarized by anti-CD43 mAbs cross-linking. We conclude that neutrophil CD43 interacts with the cytoskeleton, either directly or indirectly, to redistribute in the cell uropod under antibodies stimulation or during cell polarization by colchicine, thus highly suggesting that CD43 may be involved in cell polarization.

L20 ANSWER 44 OF 1739 MEDLINE on STN ACCESSION NUMBER: 97133428 MEDLINE DOCUMENT NUMBER: PubMed ID: 8978825

TITLE: Cell adhesion molecules NgCAM and axonin-1 form

heterodimers in the neuronal membrane and cooperate in neurite outgrowth promotion.

AUTHOR: Buchstaller A; Kunz S; Berger P; Kunz B; Ziegler U; Rader

C; Sonderegger P

CORPORATE SOURCE: Institute of Biochemistry, University of Zurich,

Switzerland.

SOURCE: Journal of cell biology, (1996 Dec) 135 (6 Pt 1) 1593-607.

Journal code: 0375356. ISSN: 0021-9525.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals OTHER SOURCE: GENBANK-Z75013

ENTRY MONTH: 199701

ENTRY DATE: Entered STN: 19970219

Last Updated on STN: 19970219 Entered Medline: 19970117

AB The axonal surface glycoproteins neuronglia cell adhesion molecule (NqCAM)

and axonin-1 promote cell-cell adhesion, neurite outgrowth and fasciculation, and are involved in growth cone guidance. A direct binding between NgCAM and axonin-1 has been demonstrated using isolated molecules conjugated to the surface of fluorescent microspheres. By expressing NgCAM and axonin-1 in myeloma cells and performing cell aggregation assays, we found that NgCAM and axonin-1 cannot bind when present on the surface of different cells. In contrast, the cocapping of axonin-1 upon antibody-induced capping of NgCAM on the surface of CV-1 cells coexpressing NgCAM and axonin-1 and the selective chemical cross-linking of the two molecules in low density cultures of dorsal root ganglia neurons indicated a specific and direct binding of axonin-1 and Ng-CAM in the plane of the same membrane. Suppression of the axonin-1 translation by antisense oligonucleotides prevented neurite outgrowth in dissociated dorsal root ganglia neurons cultured on an NgCAM substratum, indicating that neurite outgrowth on NgCAM substratum requires axonin-1. Based on these and previous results, which implicated NgCAM as the neuronal receptor involved in neurite outgrowth on NgCAM substratum, we concluded that neurite outgrowth on an NgCAM substratum depends on two essential interactions of growth cone NgCAM: a trans-interaction with substratum NgCAM and a cis-interaction with axonin-1 residing in the same growth cone membrane.

L20 ANSWER 50 OF 1739 MEDLINE on STN 97071908 ACCESSION NUMBER: MEDLINE PubMed ID: 8914753 DOCUMENT NUMBER:

Evidence for the presence of immunoglobulin E TITLE:

antibodies specific to the cell wall

phosphomannoproteins of Candida albicans in patients with

allergies.

Kanbe T; Morishita M; Ito K; Tomita K; Utsunomiya K; AUTHOR:

Ishiquro A

CORPORATE SOURCE: Laboratory of Medical Mycology, Nagoya University School of

Medicine, Japan.. tkanbe@tsuru.med.nagoya.u.ac.jp

Clinical and diagnostic laboratory immunology, (1996 Nov) 3 SOURCE:

(6) 645-50.

Journal code: 9421292. ISSN: 1071-412X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199702

ENTRY DATE: Entered STN: 19970305

> Last Updated on STN: 19970305 Entered Medline: 19970218

To determine the major antigenic component of Candida albicans against AΒ immunoglobulin E (IgE) antibodies in the sera of patients with allergies who were positive for IqE antibodies to C. albicans crude antigen in a CAP system, phosphomannoproteins (CAMP/A or CAMP/B for serotype A or B strain, respectively) and their acid-stable portions (CAMP-S/A or CAMP-S/B) were isolated from beta-mercaptoethanol (2-ME) extracts of C. albicans cells of serotypes A and B, and IqE antibodies against these components were compared with those against protein complex and enolase (CAE) fractions isolated from C. albicans cells. The dot blot test, which was used to detect IqE antibodies to the C. albicans antigens, showed that IgE antibodies to the 2-ME extract and phosphomannoprotein fractions were present in the sera of 98.0% (2-ME extract), 96.8% (CAMP/A), 93.2% (CAMP-S/A), 97.2% (CAMP/B), and 81.5% (CAMP-S/B) of the patients, whereas IgE antibodies to the protein complex and CAE fractions were found in the sera of 73.6 and 48.8% of the patients, respectively. The extent of IgE binding to the 2-ME extract and phosphomannoproteins was well correlated with the fluorescence intensities estimated with the

CAP system. Furthermore, the results obtained from the inhibition experiment with the CAP system indicated that the binding of IgE antibodies to Candida antigens is strongly inhibited by the phosphomannoprotein fraction and is an indication that the serum of the patients contained IgE antibodies specific to the cell wall phosphomannoproteins of C. albicans. Finally, an initial chemical analysis indicated that the epitopes for IgE antibodies on the phosphomannoproteins is a carbohydrate portion, since the ability of CAMP/A to inhibit the binding of IgE antibodies to the homologous CAMP/A was destroyed after oxidation by sodium periodate but not after digestion with proteinase K.

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- => head (s) differ? (s) epitope L2 16 HEAD (S) DIFFER? (S) EPITOPE
- => t ti 13 1-12
- L3 ANSWER 1 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New bispecific antibodies that bind two different targets, useful for diagnosing, preventing or treating diseases such as a hyperproliferative (e.g. cancer), cardiovascular, neurodegenerative, metabolic or an autoimmune disease.
- ANSWER 2 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

  Detecting a cancer cell in a subject sample, also related to cancer treatments, comprises determining the level of nucleic acid that is linked to map position 8q22.3 of the human genome or its expression product.
- L3 ANSWER 3 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- New purified thrombospondin fragment extracted from a body fluid, useful for diagnosing cancer e.g. adenoma, adenocarcinoma, carcinoma, lymphoma or leukemia or as calibrators, indicators, immunogens and analytes.

- L3 ANSWER 4 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Selecting an antibody from a phage display library using sequential antigen panning, useful for treating or reducing infections, such as bacterial, virus and parasitic infection, and for inhibiting cancers.
- L3 ANSWER 5 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Diagnosing and/or treating cancer, such as brain, lymphatic, liver, stomach, testicular, cervical, endometrial, renal, lung and ovarian cancers, leukemia and melanoma, comprises using soluble MIC polypeptides as markers.
- L3 ANSWER 6 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Preventing, treating or managing cancer in a patient comprises administering to the patient VITAXIN or an antibody or its fragment that competes with VITAXIN for binding to Integrin alphavbeta3 and one or more other cancer therapies.
- L3 ANSWER 7 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- Nanoparticle useful as synthetic vaccine, comprises carrier, and ligands displayed on the carrier, where ligands form polyvalent binding unit to produce interaction between nanoparticle and receptors on target.
- L3 ANSWER 8 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New Major Histocompatibility Complex (MHC) molecule construct, useful for treating, preventing, stabilizing or alleviating a disease involving MHC recognizing cells e.g., cancer.
- L3 ANSWER 9 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Epitopes formed by non-covalent association of conjugates, useful in therapeutic, prophylactic or diagnostic methods.
- L3 ANSWER 10 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Inducing human immunodeficiency virus-specific helper T-cell responses.
- L3 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 1
- TI Plakophilin, armadillo repeats, and nuclear localization.
- L3 ANSWER 12 OF 12 MEDLINE on STN DUPLICATE 2
- TI Differential localization of two epitopes of Escherichia coli ribosomal protein L2 on the large ribosomal subunit by immune electron microscopy using monoclonal antibodies.

# => d ibib abs 13 9

L3 ANSWER 9 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-102938 [11] WPIDS

DOC. NO. NON-CPI: N2001-076388 DOC. NO. CPI: C2001-030197

TITLE: Epitopes formed by non-covalent association of

conjugates, useful in therapeutic, prophylactic or

diagnostic methods.

DERWENT CLASS: B04 S03

INVENTOR(S): NEW, R; TOTH, I

PATENT ASSIGNEE(S): (PROX-N) PROXIMA CONCEPTS LTD; (MOZA-N) MOZAICO DISCOVERY

LTD; (MOZA-N) MOZAIC DISCOVERY LTD; (PROV-N) PROVALIS UK

LTD

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2001001140 A1 20010104 (200111) \* EN 39 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW AU 2000056923 A 20010131 (200124) BR 2000012002 A 20020312 (200226) EP 1190255 A1 20020327 (200229) EN R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI CN 1359469 A 20020717 (200268) KR 2002042537 A 20020605 (200277)

29

### APPLICATION DETAILS:

AU 775310

| PATENT NO     | KIND | APPLICATION     | DATE     |
|---------------|------|-----------------|----------|
| WO 2001001140 | A1   | WO 2000-GB2465  | 20000627 |
| AU 2000056923 | Α    | AU 2000-56923   | 20000627 |
| BR 2000012002 | Α    | BR 2000-12002   | 20000627 |
|               |      | WO 2000-GB2465  | 20000627 |
| EP 1190255    | A1   | EP 2000-942216  | 20000627 |
|               |      | .WO 2000-GB2465 | 20000627 |
| CN 1359469    | Α    | CN 2000-809653  | 20000627 |
| KR 2002042537 | Α    | KR 2001-716715  | 20011227 |
| JP 2003503424 | W    | WO 2000-GB2465  | 20000627 |
|               |      | JP 2001-507094  | 20000627 |
| AU 775310     | B2   | AU 2000-56923   | 20000627 |

### FILING DETAILS:

| PATENT NO     | KIND                       | PATENT NO                      |  |  |
|---------------|----------------------------|--------------------------------|--|--|
| AU 2000056923 | A Based on                 | WO 2001001140                  |  |  |
| BR 2000012002 | A Based on                 | WO 2001001140                  |  |  |
| EP 1190255    | Al Based on                | WO 2001001140                  |  |  |
| JP 2003503424 | W Based on                 | WO 2001001140                  |  |  |
| AU 775310     | B2 Previous Publ. Based on | AU 2000056923<br>WO 2001001140 |  |  |

PRIORITY APPLN. INFO: GB 1999-15074 19990628

JP 2003503424 W 20030128 (200309)

B2 20040729 (200472)

AN 2001-102938 [11] WPIDS AB

WO 200101140 A UPAB: 20010224

NOVELTY - Epitopes are formed by non-covalent association of conjugates, and assemblies composed of combinations of different head groups can elicit biological responses or participate in binding with biological receptors that assemblies of single head groups cannot.

DETAILED DESCRIPTION - A composition for interacting with a ligand comprises a non-covalent association of different conjugates, each conjugate comprising a head group and a tail group, where the tail groups form a hydrophobic aggregation and the conjugates are movable within the association so that, in the presence of a ligand, at least 2 of the head groups are appropriately positioned to form an epitope capable of interacting with the ligand more strongly than each of the head groups individually. An INDEPENDENT CLAIM is included for the following:

(a) preparation of the composition; and

(b) a method for producing a molecule for interacting with a ligand, comprising producing a composition as above; identifying the head groups which form an epitope for the ligand; and producing a molecule incorporating the functional groups of the head groups, optionally spaced apart by 1 or more linker groups so that the molecule is capable of interacting with the ligand more strongly than each of the head groups individually.

 $\ensuremath{\mathsf{USE}}$  - The compositions are useful in the rapeutic, prophylactic or diagnostic methods.

ADVANTAGE - Strong specific binding interactions can be achieved with conjugates in which the head groups are small compared to conventional biological receptors, e.g. if the head group is an oligo-peptide, then the length of the peptide chain would be at most 10 (preferably at most 6) amino acids, and compositions can be made less immunogenic than their protein counterparts.

Dwg.0/2

### => d ibib abs 13 1-8, 10-12

L3 ANSWER 1 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-091969 [10] WPIDS

DOC. NO. CPI:

C2005-031094

TITLE:

New bispecific antibodies that bind two different targets, useful for diagnosing, preventing or treating diseases such as a hyperproliferative (e.g. cancer), cardiovascular, neurodegenerative, metabolic or an

autoimmune disease.

DERWENT CLASS:

B04 D16

108

INVENTOR(S):

HANSEN, H J; MCBRIDE, W J; QU, Z

PATENT ASSIGNEE(S):

(IMMU-N) IMMUNOMEDICS INC

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LA | PG |
|-----------|-----------|------|----|----|
|           |           |      |    |    |

WO 2005004809 A2 20050120 (200510) \* EN 163

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ
OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
US UZ VC VN YU ZA ZM ZW

US 2005100543 A1 20050512 (200532)

# APPLICATION DETAILS:

| PATENT NO                      | KIND                 | APPLICATION  | DATE                             |  |  |
|--------------------------------|----------------------|--|----------------------------------|--|--|
| WO 2005004809<br>US 2005100543 | A2<br>Al Provisional | WO 2004-US20995<br>US 2003-483832P<br>US 2004-882151 | 20040701<br>20030701<br>20040701 |  |  |

PRIORITY APPLN. INFO: US 2003-483832P 20030701; US

2004-882151 20040701

AN 2005-091969 [10] WPIDS

AB W02005004809 A UPAB: 20050211

NOVELTY - A bispecific antibody comprising the structure (IgG1)-(scFv)2, is new. The antibody comprises a pair of heavy chains and a pair of light chains, where each heavy chain comprises an IgG1 heavy chain and an scFv,

where the scFv is fused to the C-terminus of the IgGl heavy chain, optionally via a linker peptide.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) a binding complex comprising a tetravalent binding molecule bound to a targetable construct, where the tetravalent binding molecule comprises 2 binding sites for a carrier epitope and 2 binding sites for a target epitope, and where the targetable construct comprises a molecular scaffold and at least 2 carrier epitopes;
  - (2) treating a disease in a subject;
  - (3) diagnosing/detecting a disease in a subject;
- (4) a kit comprising a tetravalent binding molecule comprising 2 binding sites for a carrier epitope and 2 binding sites for a target epitope; optionally, a clearing agent; and a targetable construct comprising a molecular scaffold and at least 2 carrier epitopes; and
- (5) a pharmaceutical composition comprising the bispecific antibody cited above.

ACTIVITY - Cytostatic; Cardiovascular-Gen.; Neuroprotective; Endocrine-Gen.; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The composition and methods are useful for diagnosing, preventing or treating diseases such as a hyperproliferative disease, pathogenic disease, cancer, cardiovascular disease, neurodegenerative disease, metabolic disease, or autoimmune disease. Dwa.0/8

ANSWER 2 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER:

2004-248472 [23] WPIDS

CROSS REFERENCE:

2004-315574 [29]

DOC. NO. NON-CPI: DOC. NO. CPI:

N2004-197115 C2004-097127

TITLE:

Detecting a cancer cell in a subject sample, also related to cancer treatments, comprises determining the level of nucleic acid that is linked to map position 8q22.3 of the

human genome or its expression product.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

CLANCY, J; HENDERSON, M; HENSHALL, S; O'BRIEN, P; SAUNDERS, D; SUTHERLAND, R; WATTS, C; OBRIEN, P

PATENT ASSIGNEE(S):

(GARV-N) GARVAN INST MEDICAL RES

COUNTRY COUNT:

PATENT INFORMATION:

| PA'  | TENT | NO   |      |    | KI      | 1D I | TAC  | <b>.</b><br>∑ | ī   | WEE  | K                      |          | LΑ         | ]             | PG |    |    |    |    |    |    |    |    |
|------|------|------|------|----|---------|------|------|---------------|-----|------|------------------------|----------|------------|---------------|----|----|----|----|----|----|----|----|----|
| WO   | 200  | 4022 | 2750 | )  | A1      | 200  | 0403 | 318           | (20 | 0042 | 23)                    | <br>* E1 | <b>1</b> : | 331           | -  |    |    |    |    |    |    |    |    |
|      | RW:  | ΑT   | BE   | BG | CH      | CY   | CZ   | DE            | DK  | EΑ   | $\mathbf{E}\mathbf{E}$ | ES       | FI         | FR            | GB | GH | GM | GR | HU | ΙE | IT | KE | LS |
|      |      | LU   | MC   | MW | MZ      | NL   | OA   | PT            | RO  | SD   | SE                     | SI       | SK         | $\mathtt{SL}$ | SZ | TR | TZ | ŪĞ | zM | ZW |    |    |    |
|      | W:   | ΑE   | AG   | AL | AM      | ΑT   | AU   | ΑZ            | BA  | BB   | BG                     | BR       | BY         | ΒZ            | CA | CH | CN | CO | CR | CU | CZ | DE | DK |
|      |      | DM   | DZ   | EC | EE      | ES   | FΙ   | GB            | GD  | GE   | GH                     | GM       | HR         | HU            | ID | IL | IN | IS | JP | KE | KG | KP | KR |
|      |      | ΚZ   | LC   | LK | LR      | LS   | LT   | LU            | LV  | MA   | MD                     | MG       | MK         | MN            | MW | MX | ΜZ | NI | NO | NZ | OM | PG | PH |
|      |      | PL   | PT   | RO | RU      | sc   | SD   | SĒ            | SG  | SK   | $\mathtt{SL}$          | SY       | ТJ         | TM            | TN | TR | TT | TZ | UA | UG | US | UZ | VC |
|      |      | VN   | YU   | ZA | $z_{M}$ | zw   |      |               |     |      |                        |          |            |               |    |    |    |    |    |    |    |    |    |
| 7117 | 200  | 2257 | 7776 | :  | 7.1     | 201  | 1403 | 220           | 101 | 2011 | - 0 \                  |          |            |               |    |    |    |    |    |    |    |    |    |

A1 20040329 (200459) AU 2003257275

A1 20050615 (200539) EN EP 1539957

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

# APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
|               |      |                |          |
| WO 2004022750 | A1   | WO 2003-AU1164 | 20030905 |

AU 2003257275 A1 AU 2003-257275 20030905 EP 1539957 A1 EP 2003-793494 20030905 WO 2003-AU1164 20030905

#### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2003257275 | Al Based on | WO 2004022750 |
| EP 1539957    | Al Based on | WO 2004022750 |

PRIORITY APPLN. INFO: US 2002-425218P 20021107; AU 20020905 2002-951346

2004-248472 [23] AN WPIDS

2004-315574 [29] CR

AΒ WO2004022750 A UPAB: 20050621

> NOVELTY - Detecting a cancer cell in a subject comprises determining the level of nucleic acid (Edd) that is linked to map position 8q22.3 of the human genome or its expression product in a sample of the subject, where an elevated level of the nucleic acid or polypeptide is indicative of cancer in the subject.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) a method for diagnosing a cancer or predicting recurrence of a cancer in a subject comprising determining the level of mRNA or protein encoded by nucleic acid as cited above;
  - (2) the isolated nucleic acid molecule for detecting cancer cell;
  - (3) an isolated or recombinant protein complex;
  - (4) an antibody that binds to the protein complex;
- (5) a kit for detecting or producing a protein complex, comprising an EDD polypeptide or a portion of an EDD polypeptide and a second polypeptides selected from a protein having tumor suppressor activity, a protein having cell cycle modulatory activity, a protein associated with DNA repair or damage, a nuclear targeting protein, and a progesterone receptor protein or its portion, where the portion of the second polypeptide is sufficient to bind to the EDD polypeptide or the portion of an EDD polypeptide;
  - (6) methods for isolating the protein complex;
- (7) a method for determining a predisposition for disease, or disease
- (8) a method for determining a modulator of the activity, formation or stability of an isolated or recombinant protein complex;
- (9) a method for determining a modulator of the level of protein complex formation;
- (10) a method for treating a condition associated with elevated expression of EDD protein in a cell;
- (11) an antisense nucleic acid, ribozyme, PNA, interfering RNA or siRNA; and
- (12) a pharmaceutical composition comprising the antisense nucleic acid, ribozyme, PNA, interfering RNA or siRNA.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The methods and modulator are useful for treating a condition associated with EDD over expression such as cancer, e.g. squamous cell carcinoma, hepatocellular carcinoma, ovarian cancer, breast cancer, melanoma, head and neck cancer, adenocarcinoma, squamous lung cancer, gastrointestinal cancer (e.g. gastric, colon, or pancreatic cancer), renal cell cancer, bladder cancer, prostate cancer, non-squamous carcinoma, glioblastoma and medulloblastoma. The components and composition are useful for reducing the expression of EDD in a cell to inhibit cellular proliferation (all claimed). Dwg.0/29

L3 ANSWER 3 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-226901 [21] WPIDS

DOC. NO. CPI: C2004-089523

calibrators in

New purified thrombospondin fragment extracted from a body fluid, useful for diagnosing cancer e.g. adenoma, adenocarcinoma, carcinoma, lymphoma or leukemia or as calibrators, indicators, immunogens and analytes.

DERWENT CLASS: B04 D16

INVENTOR(S): WILLIAMS, K J

PATENT ASSIGNEE(S): (WILL-I) WILLIAMS K J

COUNTRY COUNT: 105

PATENT INFORMATION:

TITLE:

| PATENT NO | KIND DATE | WEEK | LA | PG |
|-----------|-----------|------|----|----|
|           |           |      |    |    |

WO 2004018995 A2 20040304 (200421)\* EN 76

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC

VN YU ZA ZM ZW

US 2004053392 Al 20040318 (200421) AU 2003262727 Al 20040311 (200457) US 2005065324 Al 20050324 (200526)

## APPLICATION DETAILS:

| KIND           | APPLICATION                         | DATE  |
|----------------|-------------------------------------|---|
| A2             | WO 2003-US26023                     | 20030820  |
| Al Provisional | US 2002-405494P                     | 20020823  |
|                | US 2003-419462                      | 20030421  |
| A1             | AU 2003-262727                      | 20030820  |
| Al Provisional | US 2002-405494P                     | 20020823  |
| CIP of         | US 2003-419462                      | 20030421  |
|                | US 2004-782968                      | 20040220  |
|                | A2 Al Provisional Al Al Provisional | A2 WO 2003-US26023 A1 Provisional US 2002-405494P US 2003-419462 A1 AU 2003-262727 A1 Provisional US 2002-405494P CIP of US 2003-419462 |

# FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               |             |               |
| AU 2003262727 | Al Based on | WO 2004018995 |

PRIORITY APPLN. INFO: US 2003-419462 20030421; US

2002-405494P 20020823

AN 2004-226901 [21] WPIDS

AB W02004018995 A UPAB: 20040326

NOVELTY - A purified thrombospondin fragment that has been extracted from a bodily fluid, where the fragment is within a molecular weight range selected from  $80-10~\mathrm{kDa}$ ,  $40-60~\mathrm{kDa}$  or  $20-35~\mathrm{kDa}$ , and where the size in kDa is determined by gel electrophoresis after disulfide bond reduction, is new.

DETAILED DESCRIPTION - A thrombospondin fragment or its portion comprising:

- (a) one that starts between amino acyl residues N-230 and G-253 inclusive and ends between amino acyl residues V-400 and S-428;
- (b) one that starts between amino acyl residues N-230 and G-253, inclusive and ends between amino acyl residues D-527 and S-551;
  - (c) one that starts between amino acyl residues N-230 and G-253,

inclusive and ends between amino acyl residues G-787 and V-811;

- (d) one that starts between amino acyl residues I-165 and V-263, inclusive and ends between amino acyl residues K-412 and 1-530;
- (e) one that starts between amino acyl residues 1-165 and V-263, inclusive, and ends between amino acyl residues 1-530 and R-733;
- (f) one that starts between amino acyl residues 1-165 and V-263, inclusive, and ends between amino acyl residues R-733 and Y-982;
- (g) one that starts between amino acyl residues I-165 and V-263, inclusive, and ends between amino acyl residues K-412 and 1-530;
- (h) one that starts between amino acyl residues 1-165 and V-263, inclusive, and ends between amino acyl residues 1-530 and R-733;
- (i) one that starts between amino acyl residues 1-165 and V-263, inclusive, and ends between amino acyl residues R-792 and Y-982.

The thrombospondin fragment comprises at least 4-6 contiguous amino acyl residues from the thrombospondin sequence, where the amino acid sequence of the fragment is limited to one that is outside of a thrombospondin region given above.

INDEPENDENT CLAIMS are also included for:

- (1) a molecule identical in primary structure to the compound above;
- (2) a method to detect and/or quantify a thrombospondin fragment;
- (3) a method of producing antibodies against a thrombospondin fragment comprising administering the fragment to an organism capable of producing antibodies;
- (4) a monoclonal or polyclonal antibody produced by the method of (3);
- (5) a cell line producing the monoclonal antibodies or the binding agent;
- (6) a method of producing a peptide or non-peptide binding agent against a thrombospondin fragment;
- (7) a kit for the determination of the presence of, and/or the amount of, and/or the concentration of, a thrombospondin fragment in a material taken or gathered from an organism comprising the thrombospondin fragment, a binding agent that will react with thrombospondin but not with the fragment or fragments of interest or an antibody that will react thrombospondin fragments of interest but not with thrombospondin;
- (8) a method comprising determining the amount of the unlabeled or differently labeled fragment through comparison to the results obtained from the unlabeled or differently labeled fragment;
- (9) a method to detect the presence and/or clinical course of a neoplastic disease in an individual; and
- (10) a method of producing a binding agent against a thrombospondin fragment comprising binding a phage to the thrombospondin fragment.

USE - The thrombospondin fragments are useful in diagnostic methods for cancer, as method calibrators, method indicators, as immunogens and as analytes for methods with sustained clinical utility. Cancer is selected from adenoma, adenocarcinoma, carcinoma, lymphoma, leukemia, solid cancer, liquid cancer, metastatic cancer, pre-metastatic cancer, non-metastatic cancer, a cancer with vascular invasion, internal cancer, skin cancer, cancer of the respiratory system, cancer of the circulatory system, cancer of the musculoskeletal system, cancer of a muscle, cancer of a bone, cancer of a joint, cancer of a tendon or ligament, cancer of the digestive system, cancer of the liver or biliary system, cancer of the pancreas, cancer of the head, cancer of the neck, cancer of the endocrine system, cancer of the reproductive system, cancer of the male reproductive system, cancer of the female reproductive system, cancer of the genitourinary system, cancer of a kidney, cancer of the urinary tract, cancer of a sensory system, cancer of the nervous system, cancer of a lymphoid organ, blood cancer, cancer of a gland, cancer of a mammary gland, cancer of a prostate gland, cancer of an endometrial tissue, cancer of a mesodermal tissue, cancer of an ectodermal tissue, cancer of an endodermal tissue, a teratoma, a poorly-differentiated cancer, a well-differentiated cancer, and a moderately differentiated cancer.

ACCESSION NUMBER:

ANSWER 4 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

2004-011801 [01] WPIDS

DOC. NO. CPI:

C2004-003469

TITLE:

Selecting an antibody from a phage display library using

sequential antigen panning, useful for treating or reducing infections, such as bacterial, virus and parasitic infection, and for inhibiting cancers.

DERWENT CLASS: B04 D16

INVENTOR(S):

DIMITROV, D S; ZHANG, M

PATENT ASSIGNEE(S):

(USSH) US DEPT HEALTH & HUMAN SERVICES; (DIMI-I) DIMITROV

D S; (ZHAN-I) ZHANG M

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LΑ | PG |
|-----------|-----------|------|----|----|
|           |           |      |    |    |

WO 2003092630 A2 20031113 (200401) \* EN

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003237187 A1 20031117 (200442) A1 20050609 (200541) US 2005123900

## APPLICATION DETAILS:

| PATENT NO                                       | KIND                       | APPLICATION  | DATE   |
|---|----------------------------|--|--|
| WO 2003092630<br>AU 2003237187<br>US 2005123900 | A2<br>A1<br>Al Provisional | WO 2003-US14292 AU 2003-237187 US 2002-378408P WO 2003-US14292 | 20030506<br>20030506<br>20020506<br>20030506 |
|   |                            | US 2005-513725   | 20050125                                     |

# FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               |             |               |
| AU 2003237187 | Al Based on | WO 2003092630 |

PRIORITY APPLN. INFO: US 2002-378408P 2005-513725

20020506; US

20050125

2004-011801 [01] AN WPIDS

AΒ WO2003092630 A UPAB: 20040102

> NOVELTY - Selecting an antibody comprising selecting an antibody from a phage display library using sequential antigen panning, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a sequential antigen panning method for selecting an antibody from a phage display library, comprising selecting phage from a phage display library using a first selecting condition, where the first selecting condition is an antigen at a known concentration, and selecting phage from the phage selected using a second selecting condition that differs from the first selecting conditions, with the proviso that this step can be repeated any number of times, each time using a different selecting conditions;
  - (2) a composition produced using any of the methods;

- (3) a composition comprising a neutralizing antibody that recognizes more than one strain of a pathogen;
- (4) an antibody to HIV envelope glycoprotein that can recognize one or more strains of HIV, comprising a 233, 228, 231, 237, 214, 210, 212 or 212 amino acid sequence (SEQ ID NO: 1-8), given in the specification, or their variants that retains the ability to bind to the same epitope to a greater or lesser extent;
  - (5) a fusion protein or conjugate comprising the antibody of (4);
- (6) a composition comprising the antibody of (4), where the toxin is Pseudomonas toxin;
- (7) an isolated or purified nucleic acid molecule comprising a sequence encoding amino acid sequence with SEQ ID NO: 1-6, or its variant that retains the ability to bind to the same epitope to a greater or lesser extent;
  - (8) a vector comprising the isolated or purified nucleic acid of (7);
- (9) a composition comprising the isolated or purified nucleic acid molecule of (7), optionally in the form of a vector;
- (10) a host cell comprising the isolated or purified nucleic acid molecule of (7), optionally in the form of a vector;
- (11) treating, inhibiting or reducing the severity of an infection in an animal, comprising administering an infection-inhibiting amount of a composition comprising an antibody produced by the method, optionally in the form of a fusion protein, where the antibody or fusion protein is optionally encoded in an isolated or purified nucleic acid molecule, which is optionally in the form of a vector and/or optionally contained within a cell, where the infection in the animal is inhibited; and
- (12) inhibiting cancer in a mammal, comprising administering an cancer-inhibiting amount of a composition comprising an antibody produced by the method, optionally in the form of a fusion protein, where the antibody or fusion protein is optionally encoded in an isolated or purified nucleic acid molecule, which is optionally in the form of a vector and/or optionally contained within a cell, where the cancer in the animal is inhibited.

ACTIVITY - Antibacterial; Virucide; Antiparasitic; Protozoacide; Fungicide; Cytostatic.

No biological data given.

MECHANISM OF ACTION - Gene-Therapy.

USE - The methods and compositions of the present invention are useful for treating, inhibiting or reducing the severity of an infection, such as bacterial, virus and parasitic infection, and for inhibiting cancers.

Dwg.0/5

ANSWER 5 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-854115 [79] WPIDS

DOC. NO. CPI: C2003-241002

TITLE: Diagnosing and/or treating cancer, such as brain, lymphatic, liver, stomach, testicular, cervical,

> endometrial, renal, lung and ovarian cancers, leukemia and melanoma, comprises using soluble MIC polypeptides as markers.

DERWENT CLASS: B04 D16

INVENTOR(S): SPIES, T; SPIES, V

PATENT ASSIGNEE(S): (HUTC-N) HUTCHINSON CANCER RES CENT FRED

COUNTRY COUNT: 103

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2003089616 A2 20031030 (200379)\* EN

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

AU 2003225093 Al 20031103 (200438)

### APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION     | DATE     |
|---------------|------|-----------------|----------|
| WO 2003089616 |      | WO 2003-US12299 | 20030422 |
| AU 2003225093 | A1   | AU 2003-225093  | 20030422 |

### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               |             |               |
| AU 2003225093 | Al Based on | WO 2003089616 |

PRIORITY APPLN. INFO: US 2002-374442P 20020422

AN 2003-854115 [79] WPIDS

AB WO2003089616 A UPAB: 20031208

NOVELTY - Assaying for cancer in a subject comprises obtaining at least a first sample from a subject suspected of having or being at risk for developing cancer, and assaying for a soluble MIC polypeptide in the sample, where identification of a soluble MIC polypeptide in the sample indicates cancer.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) assaying for cancer in a subject, comprising obtaining a sample from a subject suspected of having or being at risk for developing cancer, assaying for a soluble MIC polypeptide in the sample comprising contacting a sample from the subject with a first antibody attached to a solid support, wherein the first antibody binds to a soluble MIC polypeptide in the sample, and incubating the sample with a second antibody, wherein the second antibody binds to the soluble MIC polypeptide, wherein identification of a soluble MIC polypeptide in the sample indicates cancer;
- (2) treating cancer, comprising detecting cancer in a subject by obtaining a sample from the subject and assaying for a soluble MIC polypeptide in the sample, and administering to the subject chemotherapy, radiation therapy, gene therapy, or hormone therapy;
- (3) diagnosing or prognosing an autoimmune disease or condition in a patient, comprising identifying a patient suspected of having an autoimmune disease or condition, and assaying for a soluble MIC polypeptide in a sample from the patient, wherein identification of a soluble MIC polypeptide in the sample indicates an autoimmune disease or condition;
- (4) kit for diagnosing or prognosing cancer or an autoimmune disease in a patient, comprising, in suitable container means an agent that specifically recognizes all or part of a MIC polypeptide or a nucleic acid encoding a MIC polypeptide, and a positive control that can be used to determine whether the agent is capable of specifically recognizing all or part or a MIC polypeptide or a nucleic acid encoding a MIC polypeptide;
- (5) screening for candidate therapeutic agents for an autoimmune disease, comprising contacting a MIC polypeptide with an NKG2D receptor polypeptide in the presence and absence of a candidate substance, assaying for binding between the MIC polypeptide and the NKG2D receptor in its presence and absence, wherein a reduction of binding in its presence compared to its absence is indicative of a candidate therapeutic agent for an autoimmune disease; and

(6) assaying an candidate therapeutic agent for efficacy against an autoimmune disease, comprising contacting a MIC polypeptide with an NKG2D receptor polypeptide in the presence and absence of the candidate substance, wherein the candidate substance is substantially pure, assaying for binding between the MIC polypeptide and the NKG2D receptor in its presence and absence, wherein a reduction of binding in its presence compared to its absence indicates the candidate substance has the ability to reduce binding between the MIC polypeptide and the NKG2D receptor.

ACTIVITY - Cytostatic; Immunosuppressive; Endocrine-Gen.; Anabolic; Hypertensive; Antipsoriatic; Antirheumatic; Antiarthritic; Antiinflammatory; Dermatological.

No biological data given.

MECHANISM OF ACTION - MIC-Modulator; Gene-Therapy.

No biological data given.

USE - The methods and compositions of the present invention are useful for diagnosing, prognosticating and/or treating cancer, such as brain cancer, lymphatic cancer, liver cancer, stomach cancer, testicular cancer, cervical cancer, ovarian cancer, leukemia, melanoma, head and neck cancer, esophageal cancer, colon cancer, breast cancer, lung cancer, prostate cancer, and renal cancer, and autoimmune diseases such as alopecia, Addison's disease, psoriasis, rheumatoid arthritis and systemic lupus erythematosis.

Dwg.0/2

L3 ANSWER 6 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-748337 [70] WPIDS

CROSS REFERENCE: 2003-748311 [70]; 2004-604159 [58]

DOC: NO. NON-CPI: N2003-599814 DOC: NO. CPI: C2003-205213

TITLE: Preventing, treating or managing cancer in a patient comprises administering to the patient VITAXIN or an antibody or its fragment that competes with VITAXIN for

antibody or its fragment that competes with VITAXIN for binding to Integrin alphavbeta3 and one or more other

cancer therapies.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): DORMITZER, M; HEINRICHS, J; KIENER, P; WALSH, W;

WOESSNER, R

MC MK NL PT RO SE SI SK TR

PATENT ASSIGNEE(S): (MEDI-N) MEDIMMUNE INC

COUNTRY COUNT: 103

PATENT INFORMATION:

| PAT | rent          | NO   |      |    | KI          | ND I | DATI | Ξ   | Ţ             | VEE  | K    |        | LA | ]             | PG |    |    |    |    |    |    |    |    |
|-----|---------------|------|------|----|-------------|------|------|-----|---------------|------|------|--------|----|---------------|----|----|----|----|----|----|----|----|----|
| WO  | WO 2003075957 |      |      |    | A1 20030918 |      |      | (20 | (200370) * 1  |      |      | EN 155 |    |               |    |    |    |    |    |    |    |    |    |
|     | RW:           | ΑT   | ΒE   | BG | CH          | CY   | CZ   | DE  | DK            | EA   | EE   | ES     | FI | FR            | GB | GH | GM | GR | HU | ΙE | ΙT | KE | LS |
|     |               | LU   | MC   | MW | MZ          | NL   | OA   | PT  | RO            | SD   | SE   | SI     | sĸ | $\mathtt{SL}$ | SZ | TR | TZ | ŬĞ | ZM | ZW |    |    |    |
|     | W:            | ΑE   | AG   | ΑL | AM          | ΑT   | AU   | ΑZ  | BA            | ВВ   | BG   | BR     | BY | BZ            | CA | CH | CN | CO | CR | CU | CZ | DE | DK |
|     |               | DM   | DZ   | EC | EE          | ES   | FI   | GB  | GD            | GE   | GH   | GM     | HR | HU            | ID | IL | IN | IS | JΡ | KE | KG | ΚP | KR |
|     |               | KZ   | LC   | LK | LR          | LS   | LT   | LU  | LV            | MA   | MD   | MG     | MK | MN            | MW | ΜX | MZ | NO | ΝZ | OM | PH | PL | PT |
|     |               | RO   | RU   | SC | SD          | SE   | SG   | SK  | $\mathtt{SL}$ | ТJ   | TM   | TN     | TR | TT            | TZ | UA | UG | US | UZ | VC | VN | YU | ZA |
|     |               | ZM   | ZW   |    |             |      |      |     |               |      |      |        |    |               |    |    |    |    |    |    |    |    |    |
| US  | 200           | 400  | 1835 | 5  | <b>A</b> 1  | 200  | 040  | 101 | (20           | 0040 | 02)  |        |    |               |    |    |    |    |    |    |    |    |    |
| ΑU  | 200           | 3217 | 7930 | )  | A1          | 200  | 0309 | 922 | (20           | 0043 | 31)  |        |    |               |    |    |    |    |    |    |    |    |    |
| EΡ  | 148           | 7492 | 2    |    | Α1          | 200  | 0412 | 222 | (20           | 0050 | )1 i | F.N    | J  |               |    |    |    |    |    |    |    |    |    |

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV

# APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |  |  |
|---------------|------|----------------|----------|--|--|
|               |      |                |          |  |  |
| WO 2003075957 | A1   | WO 2003-US6684 | 20030304 |  |  |

| U | S | 2004001835 | A1 | Provisional | US | 2002-361859P | 20020304 |
|---|---|------------|----|-------------|----|--------------|----------|
|   |   | •          |    | Provisional | US | 2002-370398P | 20020405 |
|   |   |            |    | Provisional | US | 2003-444265P | 20030130 |
|   |   |            |    |             | US | 2003-379189  | 20030304 |
| Α | U | 2003217930 | A1 |             | AU | 2003-217930  | 20030304 |
| E | P | 1487492    | A1 |             | EP | 2003-713905  | 20030304 |
|   |   |            |    |             | WO | 2003-US6684  | 20030304 |

## FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2003217930 | Al Based on | WO 2003075957 |
| EP 1487492    | Al Based on | WO 2003075957 |

PRIORITY APPLN. INFO: US 2003-444265P 20030130; US 2002-361859P 20020304; US 2002-370398P 20020405; US

2003-379189

2003-748337 [70] AN WPIDS

CR 2003-748311 [70]; 2004-604159 [58]

AΒ WO2003075957 A UPAB: 20050103

> NOVELTY - Preventing, treating or managing cancer in a patient, comprises administering to the patient VITAXIN (RTM) or its antigen-binding fragment, or an antibody or its fragment that competes with VITAXIN (RTM) for binding to Integrin alpha v beta 3 and a dose of one or more other cancer therapies.

20030304

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition;

(2) a method of screening for antibodies with specific binding affinity for the epitope specifically recognized by VITAXIN; and

(3) a method for detecting Integrin alpha v beta 3 in tissue.

ACTIVITY - Cytostatic; Fungicide; Antiparasitic; Antiemetic; Antiinflammatory; Virucide. No biological data given.

MECHANISM OF ACTION - Gene therapy; Vaccine.

USE - The method is useful for preventing, treating or managing cancer in a patient (claimed). Dwg.0/7

ANSWER 7 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER:

2003-167365 [16] C2003-043494

DOC. NO. CPI: TITLE:

Nanoparticle useful as synthetic vaccine, comprises carrier, and ligands displayed on the carrier, where

ligands form polyvalent binding unit to produce interaction between nanoparticle and receptors on target.

WPIDS

DERWENT CLASS:

B04 C06 D16

INVENTOR(S):

BARGATZE, R F; CUTLER, J E; GLEE, P M; HAN, Y; JUTILA, J

W; NAGY, J O; PASCUAL, D

PATENT ASSIGNEE(S):

(BARG-I) BARGATZE R F; (CUTL-I) CUTLER J E; (GLEE-I) GLEE P M; (HANY-I) HAN Y; (JUTI-I) JUTILA J W; (NAGY-I) NAGY J O; (PASC-I) PASCUAL D; (LIGO-N) LIGOCYTE PHARM INC;

(UYMO-N) UNIV MONTANA STATE-BOZEMAN

COUNTRY COUNT: 97

PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LA PG |
|-----------|-----------|------|-------|
|           |           |      |       |

WO 2002100325 A2 20021219 (200316) \* EN

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW US 2003223938 A1 20031204 (200380)

#### APPLICATION DETAILS:

AU 2001297913

| PATENT NO                      | KIND                            | APPLICATION   | DATE   |  |  |  |  |
|--------------------------------|---------------------------------|---|--|--|--|--|--|
| WO 2002100325<br>US 2003223938 | A2<br>Al Provisional<br>Cont of | WO 2001-US42712<br>US 2000-239874P<br>WO 2001-US42712<br>US 2003-412685 | 20011015<br>20001013<br>20011015<br>20030414 |  |  |  |  |
| AU 2001297913                  | A1                              | AU 2001-297913  | 20030414                                     |  |  |  |  |

#### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               | ~           |               |
| AU 2001297913 | Al Based on | WO 2002100325 |

A1 20021223 (200452)

PRIORITY APPLN. INFO: US 2000-239874P 20001013; US

2003-412685 20030414

AN 2003-167365 [16] WPIDS AB W02002100325 A UPAB: 20030307

NOVELTY - A nanoparticle (I) comprising a carrier, a first ligand (L1), and a second ligand (L2), that is different than L1, both displayed on the carrier, is new. L1 and L2 form a polyvalent binding unit to produce a specific interaction between the nanoparticle and receptor(s) on a target, and L2 interacts specifically with the receptor(s) based on its charge or hydrophobicity.

DETAILED DESCRIPTION - A nanoparticle (I) comprising a carrier, a first ligand (L1), and a second ligand (L2), that is different than L1, both displayed on the carrier, is new. L1 and L2 form a polyvalent binding unit to produce a specific interaction between the nanoparticle and receptor(s) on a target under physiologically relevant shear conditions, and L2 interacts specifically with the receptor(s) based on its charge or hydrophobicity.

INDEPENDENT CLAIMS are also included for the following:

- (1) a therapeutic formulation (II) in unit dose form comprising (I), to modulate a specific interaction between a cell or toxin and its receptor on a target in a host, where L1 is derived from or mimics a ligand on the cell or toxin;
- (2) a vaccine (III) comprising (I), where L1 is an epitope that is derived from a pathogen, pathogen-derived toxin or tumor cell, and the vaccine is formulated to elicit a protective immune response against that pathogen or tumor cell;
- (3) a diagnostic imaging agent comprising (I), and further comprising a contrast agent detectable by medical resonance imaging or other visualization techniques;
- (4) a delivery vehicle (IV) comprising (I), and an agent to be delivered to the target;
- (5) optimizing (V) a nanoparticle displaying polyvalent binding units having L1 and L2, comprises optimizing the amount of L1 on the nanoparticle under physiologically relevant shear conditions and holding the optimized amount of L1 constant, optimizing the amount of L2 under physiologically relevant shear conditions;
- (6) a nanoparticle library (VI) comprising multiple polymer beads, where each bead contains several nanoparticles associated with the surface of the polymer bead, where all of the nanoparticles associated with any

one bead display the same polyvalent binding unit;

- (7) a vaccine comprising (I), and a polynucleotide sequence that encodes an epitope found on a pathogen or a tumor cell and the vaccine is formulated to elicit a protective immune response against that pathogen or tumor cell; and
  - (8) a nanoparticle produced by (VI).

ACTIVITY - Antibacterial; Fungicide; Virucide; Protozoacide; Anti-HIV; Immunostimulant; Antiinflammatory; Cytostatic.

MECHANISM OF ACTION - Vaccine; Inhibitor of lymphocyte attachment in Peyer's patch.

A variation on the Peyer's patch method was used to examine the P-selectin-mediated adhesion in a mouse mesentery venule model. A lateral incision was made into the abdominal wall to allow the small intestine to be externalized. The intestine was positioned for microscopic examination of the mesentery. A solution of PMA in phosphate buffered saline was superfused directly onto the mesentery to allow for upregulation of P-selectin in the endothelium of the mesentery venules. The area of the incision was treated and cannulation of the tail vein was performed. A variable dose of carbohydrate- and sulfate-displaying nanoparticle was administered. The results showed the reduction in number of leukocyte rolling and sticking events compared to the untreated control, and the increase in cell velocity relative to the untreated control. At the highest dosage tested (2.3 mg/kg of carbohydrate), there was a greater than 65% reduction in the number of rolling/sticking leukocytes and a nearly 90% increase in the rolling velocity, over the control.

USE - (I) is useful for sequestration of toxins in the bloodstream of a host, by administering (I) to bind a circulating toxin or toxic metabolic product, where the first ligand is derived from or mimics a receptor that specifically binds to the toxin or toxic metabolic product. The binding is effective to produce an effect such as decreased inflammation, decreased systemic toxicity, chelation therapy, neutralization of pathogens, inhibition of metastasis, inhibition of drug intoxication, tissue regeneration, selective cellular differentiation and proliferation. (I) is also useful in a diagnostic method by allowing (I) to bind to a toxin or pathogen or an antibody against such toxins or pathogens and then detecting nanoparticles bound to such toxins, pathogen or antibodies. (III) is formulated to elicit a protective immune response against a pathogen such as Escherichia coli, Candida albicans, Brucella sp., Salmonella sp., Shigella sp., Pseudomonas sp., Bordetella sp., Clostridium sp., group B strep, E.coli 0157, Norwalk virus, anthrax, human immunodeficiency virus (HIV), sexually transmitted diseases (STDs), Chlamydia, hepatitis B virus (HBV), malaria, cell wall proteins of Candida sp., and GB3 toxin from E.coli 0157. (IV) is useful for delivering an agent such as therapeutic or cytotoxic agent to a target. (VI) is useful for screening agents, by adding at least one candidate agent to the nanoparticle library, and detecting binding of the agent to any one or more polymer beads in the library. The candidate agent comprises a detectable label and acts as a reporter to L1. Vaccine construct comprising (I) is useful for delivering nanoparticle therapeutic molecules to an animal (all claimed).

The polymerized nanoparticle constructs and assemblies are useful as modulators, inhibitors and enhancers and drug delivery agents for a variety of interactions as well as their down-stream effects, such as pathogen-cell attachment, pathogen-derived-toxin-cell attachment, cell-cell attachment mediated diseases, integrin adhesions, complement fixation and chemokine-mediated events. The nanoparticles are readily used as synthetic vaccines. Dwg.0/6

ANSWER 8 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN ACCESSION NUMBER: 2002-759837 [82] WPIDS DOC. NO. CPI: C2002-214753

TITLE:

New Major Histocompatibility Complex (MHC) molecule construct, useful for treating, preventing, stabilizing or alleviating a disease involving MHC recognizing cells

e.g., cancer.

DERWENT CLASS:

B04 D16

INVENTOR(S): AMELLEM, O; BUUS, S; PETERSEN, L O; RUUD, E; SCHOLLER, J;

WINTHER, L; AAMELLEM, O; RUUB, E; SCHOELLER, J

PATENT ASSIGNEE(S):

(DAKO-N) DAKO AS; (DYNA-N) DYNAL BIOTECH ASA; (DAKO-N)

DAKOCYTOMATION DENMARK AS

COUNTRY COUNT:

101

PATENT INFORMATION:

| PAT | rent            | ИО   | 10   |    |    | ND I | DATI          | Ξ   | 7             | WEE  | K                |          | LA     | ]   | PG |    |    |    |    |    |    |    |    |
|-----|-----------------|------|------|----|----|------|---------------|-----|---------------|------|------------------|----------|--------|-----|----|----|----|----|----|----|----|----|----|
| WO  | WO 2002072631 A |      |      |    | A2 | 200  | 0209          | 919 | (20           | 002  | 82) <sup>3</sup> | <br>* El | EN 304 |     |    |    |    |    |    |    |    |    |    |
|     | RW:             | ΑT   | BE   | CH | CY | DE   | DK            | EA  | ES            | FI   | FR               | GB       | GH     | GM  | GR | ΙE | IT | KE | LS | LU | MC | MW | MZ |
|     |                 | NL   | OA   | PT | SD | SE   | $\mathtt{SL}$ | SZ  | TR            | TZ   | UG               | ZM       | ZW     |     |    |    |    |    |    |    |    |    |    |
|     | W:              | ΑE   | AG   | AL | AM | ΑT   | AU            | ΑZ  | BA            | BB   | BG               | BR       | BY     | ΒZ  | CA | CH | CN | CO | CR | CU | CZ | DE | DK |
|     |                 | DM   | DZ   | EC | EE | ES   | FI            | GB  | GD            | GΕ   | GH               | GM       | HR     | HU  | ID | IL | IN | IS | JP | KE | KG | ΚP | KR |
|     |                 | ΚZ   | LC   | LK | LR | LS   | LT            | LU  | LV            | MA   | MD               | MG       | MK     | MN  | MW | MX | MZ | NO | NZ | OM | PH | PL | PT |
| •   |                 | RO   | RU   | SD | SE | SG   | SI            | SK  | $\mathtt{SL}$ | ТJ   | TM               | TN       | TR     | TT  | TZ | UA | UG | US | UZ | VN | YU | ZΑ | ZM |
|     |                 | ZW   |      |    |    |      |               |     |               |      |                  |          |        |     |    |    |    |    |    |    |    |    |    |
| ИО  | 2003            | 3004 | 1020 | )  | Α  | 200  | 0311          | 106 | (20           | 0038 | 30)              |          |        |     |    |    |    |    |    |    |    |    |    |
| EΡ  | 1377            |      |      |    |    |      |               |     | •             |      | •                | Eì       |        |     |    |    |    |    |    |    |    |    |    |
|     | R:              | AL   | ΑT   | ΒE | CH | CY   | DE            | DK  | ES            | FΙ   | FR               | GB       | GR     | ΙE  | ΙT | LI | LT | LU | LV | MC | MK | NL | PT |
|     |                 | RO   | SE   | SI | TR |      |               |     |               |      |                  |          |        |     |    |    |    |    |    |    |    |    |    |
|     | 2002            |      |      |    | A1 |      |               |     | •             |      | ,                |          |        |     |    |    |    |    |    |    |    |    |    |
| JΡ  | 2005            | 5500 | 257  | 7  | W  | 200  | )501          | 106 | (20           | 050  | 05)              |          | 4      | 139 |    |    |    |    |    |    |    |    |    |

### APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
| WO 2002072631 | A2   | WO 2002-DK169  | 20020313 |
| NO 2003004020 | Α    | WO 2002-DK169  | 20020313 |
|               |      | NO 2003-4020   | 20030911 |
| EP 1377609    | A2   | EP 2002-706685 | 20020313 |
|               |      | WO 2002-DK169  | 20020313 |
| AU 2002240818 | A1   | AU 2002-240818 | 20020313 |
| JP 2005500257 | W    | JP 2002-571544 | 20020313 |
|               |      | WO 2002-DK169  | 20020313 |

## FILING DETAILS:

| PATENT NO             | KIND                                     | PATENT NO                                       |  |  |  |  |  |
|-----------------------|--|---|--|--|--|--|--|
| AU 2002240818         | A2 Based on<br>A1 Based on<br>W Based on | WO 2002072631<br>WO 2002072631<br>WO 2002072631 |  |  |  |  |  |
| PRIORITY APPLN. INFO: | US 2001-275470P                          | 20010314; DK                                    |  |  |  |  |  |
|                       | 2001-435<br>2001-436<br>2001-441         | 20010314; DK<br>20010314; DK<br>20010314; US    |  |  |  |  |  |
|                       |  | 20010314; US<br>20010314                        |  |  |  |  |  |
| AN 2002-759837 [82]   | WPIDS                                    |   |  |  |  |  |  |

WO 200272631 A UPAB: 20021220 AB

> NOVELTY - A new Major Histocompatibility Complex (MHC) molecule construct comprising a carrier molecule to which one or more MHC molecules are attached either directly or via one or more entities, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the

following:

- (1) detecting the presence or MHC recognizing cells in a sample;
- (2) monitoring MHC recognizing cells;
- (3) establishing a prognosis of a disease involving MHC recognizing cells;
- (4) determining the status of, or the effectiveness of a medicament against, a disease involving MHC recognizing cells;
  - (5) diagnosing a disease involving MHC recognizing cells;
- (6) a therapeutic composition comprising as active ingredient a MHC molecule construct;
- (7) up-regulating, down-regulating or modulating an immune response in an animal, including a human being;
  - (8) treating an animal, including a human being;
  - (9) inducing energy of a cell in animal, including a human being;
  - (10) an adoptive cellular immunotherapeutic method;
  - (11) obtaining MHC recognizing cells; or
  - (12) producing a therapeutic composition.

ACTIVITY - Cytostatic; Antiinflammatory; Dermatological; Antiasthmatic; Antidiabetic; Anti-HIV; Virucide; Antiarteriosclerotic; Antiulcer; Antirheumatic; Antiarthritic; Antipsoriatic; Immunosuppressive. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - The MHC molecule construct is useful as a therapeutic composition in in vivo or ex vivo therapy, for treating, preventing, stabilizing or alleviating a disease involving MHC recognizing cells, for monitoring MHC recognizing cells or establishing a prognosis of a disease or diagnosing a disease, or determining the status of a disease or the effectiveness of a medicament against a disease, involving MHC recognizing cells, e.g., chronic inflammatory bowel disease such as Crohn's disease or ulcerative colitis, sclerosis, type I diabetes, rheumatoid arthritis, psoriasis, atopic dermatitis, asthma, malignant melanoma, renal carcinoma, breast cancer, lung cancer, cancer of the uterus, cervical cancer, prostate cancer, brain cancer, head and neck cancer, leukemia, cutaneous lymphoma, hepatic carcinoma, colorectal cancer, bladder cancer, rejection-related disease, Graft-versus-host-related disease, or a viral disease associated with hepatitis, Acquired Immunodeficiency Syndrome (AIDS), measles, pox, chicken pox, rubella or herpes. The MHC molecule construct is also useful for flow cytometric, histological or cytological method (all claimed.) Dwg.0/57

L3 ANSWER 10 OF 12 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 1999-610208 [52] WPIDS

DOC. NO. CPI: C1999-177599

TITLE: Inducing human immunodeficiency virus-specific helper

T-cell responses.

DERWENT CLASS: B04 D16
INVENTOR(S): WALKER, B D

PATENT ASSIGNEE(S): (GEHO) GEN HOSPITAL CORP

COUNTRY COUNT:

PATENT INFORMATION:

| PATENT NO  | KII | ND DATE  | WEEK      | LΑ | PG |
|------------|-----|----------|-----------|----|----|
|            |     |          | <b></b>   |    |    |
| US 5972339 | Α   | 19991026 | (199952)* | 2  | 5  |

## APPLICATION DETAILS:

| PATENT NO  | KIND | APPLICATION    | DATE     |
|------------|------|----------------|----------|
|            |      |                |          |
| US 5972339 | Α    | US 1997-969721 | 19971113 |

PRIORITY APPLN. INFO: US 1997-969721 19971113

AN 1999-610208 [52] WPIDS

AB US 5972339 A UPAB: 19991210

NOVELTY - A method (X) for producing human immunodeficiency virus (HIV)-specific helper T-cell responses in animals using helper T-cell epitopes of peptides 112, 117, 118, 120, 121, 122, 125 and/or 127, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(i) a method (X) for producing a human immunodeficiency virus (HIV)-specific helper T-cell response in an animal, comprising:

- (1) providing a polypeptide 8 to 50 amino acid residues in length comprising a helper T-cell epitope of the HIV capsid (which produces a stimulation index more than 10 in CD4+ cells in a subject chronically infected with HIV); and
- (2) administering the polypeptide to produce a HIV-specific helper T-cell response; and
  - (ii) a composition (Y) comprising:
- (1) a polypeptide 8 to 50 amino acid residues in length, comprising a helper T-cell epitope of peptide 112, 117, 118, 120, 121, 122, 125 and/or 127 (which have defined amino acid sequences ((I) -(VIII)) given in the specification); and

(2) an adjuvant.

ACTIVITY - Anti-HIV.

MECHANISM OF ACTION - Vaccine.

USE - (X) may be used for inducing HIV-specific helper T-cell responses in animals (preferably humans), especially those already chronically infected with HIV (i.e. inducing immunity by vaccination). Dwg.0/5

L3 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 1999220994 MEDLINE DOCUMENT NUMBER: PubMed ID: 10206153

TITLE: Plakophilin, armadillo repeats, and nuclear localization.

AUTHOR: Klymkowsky M W

CORPORATE SOURCE: Molecular, Cellular and Developmental Biology, University

of Colorado, Boulder 80309-0347, USA..

klym@spot.colorado.edu

CONTRACT NUMBER: GM54001 (NIGMS)

SOURCE: Microscopy research and technique, (1999 Apr 1) 45 (1)

43-54.

Journal code: 9203012. ISSN: 1059-910X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199907

ENTRY DATE: Entered STN: 19990816

Last Updated on STN: 19990816 Entered Medline: 19990730

Plakophilins are armadillo-repeat containing proteins, identified through their localization to desmosomes. Expressed in a wide range of tissues, plakophilins are largely nuclear in most cell types [Schmidt et al. (1997) Cell Tissue Res 290:481; Mertens et al. (1996) J. Cell Biol 135:1009]. Using Xenopus embryos and cultured A6 cells, together with myc- and green fluorescent protein (GFP)-tags, we found that both the N-terminal, non-armadillo repeat "head" and the C-terminal armadillo repeat-containing regions can enter nuclei. The "arm" repeat domain is predominantly cytoplasmic and concentrated at the cell cortex, whereas the head and full-length polypeptides are concentrated in the nucleus. The head domain can also be seen to decorate and disrupt keratin filament network organization in some cells. In the course of these studies, we found that

the distribution of the myc-epitope and green fluorescence differed in fixed cells, e.g., while the green fluorescence of a myc- and GFP-tagged head domain polypeptide was usually exclusively nuclear, a substantial fraction of the myc-immunoreactivity was cytoplasmic. Treating cells with the translation inhibitor cycloheximide reduces the cytoplasmic myc-signal, suggesting that it represented nascent polypeptides awaiting folding and nuclear import. Based on these types of experiments, GFP can be seen as a marker of the distribution of the mature form of the tagged polypeptide.

L3 ANSWER 12 OF 12 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 91107695 MEDLINE DOCUMENT NUMBER: PubMed ID: 1703157

TITLE: Differential localization of two epitopes of Escherichia

coli ribosomal protein L2 on the large ribosomal subunit by

immune electron microscopy using monoclonal antibodies.

AUTHOR: Olson H M; Nag B; Etchison J R; Traut R R; Glitz D G

CORPORATE SOURCE: Department of Biological Chemistry and Molecular Biology

Institute, UCLA School of Medicine, University of

California 90024.

CONTRACT NUMBER: GM 17924 (NIGMS)

GM 32769 (NIGMS)

SOURCE: Journal of biological chemistry, (1991 Jan 25) 266 (3)

1898-902.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199102

ENTRY DATE: Entered STN: 19910329

Last Updated on STN: 19980206 Entered Medline: 19910227

Two monoclonal antibodies (mAb), directed toward different epitopes of Escherichia coli ribosomal protein L2, have been used as probes in immune electron microscopy. mAb 5-186 recognizes an epitope within residues 5-186 of protein L2; it is seen to bind to 50 S subunits at or near the peptidyl transferase center, beside the subunit head on the L1 shoulder. mAb 187-272 recognizes an epitope within residues 187-272. This antibody binds to the face of the 50 S subunit, below the head and slightly toward the side with the stalk; this site is near the translocation domain. Both antibodies can bind simultaneously to single subunits. This indicates that protein L2 is elongated, reaching from the peptidyl transferase center to below the subunit head and approaching the translocational domain. The different locations of the two epitopes are consistent with previous biochemical results with the two antibodies (Nag, B., Tewari, D. S., Etchison, J. R., Sommer, A., and Traut, R. R. (1986) J. Biol. Chemical 261, 13892-13897).

=> d his

(FILE 'HOME' ENTERED AT 15:58:16 ON 22 JUL 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 15:58:37 ON 22 JUL 2005

L1 10 HEAD (S) DIFFERENT (S) EPITOPE
L2 16 HEAD (S) DIFFER? (S) EPITOPE
L3 12 DUP REM L2 (4 DUPLICATES REMOVED)

=> head (s) differ? (s) (ligand or receptor)

- => (head (s) differ? (s) (ligand or receptor)) and tail L5 26 (HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)) AND TAIL
- => dup rem 15
  PROCESSING COMPLETED FOR L5
  L6 15 DUP REM L5 (11 DUPLICATES REMOVED)
- => t ti 16 1-15
- L6 ANSWER 1 OF 15 MEDLINE on STN DUPLICATE 1
- TI Membrane-proximal {alpha}/{beta} stalk interactions differentially regulate integrin activation.
- L6 ANSWER 2 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Determining whether treatment of a disorder with histone deacetylase inhibitors is to be started/continued or not, using antibody capable of binding to acetylated histone but not to deacetylated histone.
- L6 ANSWER 3 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Nanoparticle useful as synthetic vaccine, comprises carrier, and ligands displayed on the carrier, where ligands form polyvalent binding unit to produce interaction between nanoparticle and receptors on target.
- L6 ANSWER 4 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Epitopes formed by non-covalent association of conjugates, useful in therapeutic, prophylactic or diagnostic methods.
- L6 ANSWER 5 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Detecting heterogeneous nucleic acid sequences in organisms and cells, useful for detecting and identifying genetically modified organisms or their products.
- L6 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- Preparation and electrochemical behavior of dinuclear platinum complexes containing NCN ligands (NCN = [C6H3(Me2NCH2)2-2,6]-). The crystal structure of [C6H3(Me2NCH2)2-1,3-(C.tplbond.C)-5]2
- L6 ANSWER 7 OF 15 MEDLINE on STN DUPLICATE 2
- TI The influence of stereoisomerism on the pharmacokinetics of Tc radiopharmaceuticals.
- L6 ANSWER 8 OF 15 MEDLINE on STN DUPLICATE 3
- TI Selective targeting of human cells by a chimeric adenovirus vector containing a modified fiber protein.
- L6 ANSWER 9 OF 15 MEDLINE on STN DUPLICATE 4
- TI Ligand recruitment by vinculin domains in transfected cells.
- L6 ANSWER 10 OF 15 MEDLINE on STN DUPLICATE 5
- TI Synthesis and biological evaluation of a new reversely linked type of dual histamine H2 and gastrin receptor antagonist.
- L6 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Synthesis and Characterization of Poly(benzoyl-1,4-phenylene)s. 2. Catalyst Coligand Effects on Polymer Properties
- L6 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Cytosine nucleobase as a tridentate ligand: metal binding to N(3), N(4)
  and O(2) in trans-[(NH2Me)2Pt(dmcyt)2Ag2][NO3]2 (dmcyt =
  1,5-dimethylcytosinate)

- L6 ANSWER 13 OF 15 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
- TI CHARACTERIZATION OF 5-HT RECEPTOR SUBTYPES INVOLVED IN THE MOTOR BEHAVIORS PRODUCED BY INTRATHECAL ADMINISTRATION OF 5-HT AGONISTS IN RATS.
- L6 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2005 ACS on STN
- TI X-ray crystal structure and homonuclear phosphorus-31-phosphorus-31 o/J-resolved NMR spectroscopic studies of tetrakis (1,8-diisocyanomethane)bis(triphenylphosphine)diirdium silver(3+) tris(hexafluorophosphate). Observation of a statistical mixture of "head/tail" isomers
- L6 ANSWER 15 OF 15 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
- TI The regional distribution of a morphine like factor enkephalin in monkey brain.

### => d ibib abs 16 1-3, 5

L6 ANSWER 1 OF 15 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2005329024 IN-PROCESS

DOCUMENT NUMBER: PubMed ID: 15863495

TITLE: Membrane-proximal {alpha}/{beta} stalk interactions

differentially regulate integrin activation.

AUTHOR: Kamata Tetsuji; Handa Makoto; Sato Yukiko; Ikeda Yasuo;

Aiso Sadakazu

CORPORATE SOURCE: Departments of Anatomy, Transfusion Medicine and Cell

Therapy, and Internal Medicine, Keio University School of Medicine, Tokyo 160-8582, Japan.. kamata@sc.itc.keio.ac.jp

SOURCE: Journal of biological chemistry, (2005 Jul 1) 280 (26)

24775-83. Electronic Publication: 2005-04-29.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

rob. Countri: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20050628

Last Updated on STN: 20050715

- AB The affinity of integrin-ligand interaction is regulated extracellularly by divalent cations and intracellularly by inside-out signaling. We report here that the extracellular, membrane-proximal alpha/beta stalk interactions not only regulate cation-induced integrin activation but also play critical roles in propagating inside-out signaling. Two closely related integrins, alphaIIbbeta3 and alphaVbeta3, share high structural homology and bind to similar ligands in an RGD-dependent manner. Despite these structural and functional similarities, they exhibit distinct responses to Mn(2+). Although alphaVbeta3 showed robust ligand binding in the presence of Mn(2+), alphaIIbbeta3 showed a limited increase but failed to achieve full activation. Swapping alpha stalk regions between alphaIIb and alphaV revealed that the alpha stalk, but not the ligand -binding head region, was responsible for the difference
  - . A series of alphaIIb/alphaV domain-swapping chimeras were constructed to identify the responsible domain. Surprisingly, the minimum component required to render alphaIIbbeta3 susceptible to Mn(2+) activation was the alphaV calf-2 domain, which does not contain any divalent cation-binding sites. The calf-2 domain makes interface with beta epidermal growth factor 4 and beta tail domain in three-dimensional structure. The effect of calf-2 domain swapping was partially reproduced by mutating the specific amino acid residues in the calf-2/epidermal growth factor 4-beta tail domain interface. When this interface was

constrained by an artificially introduced disulfide bridge, the Mn(2+)-induced alphaVbeta3-fibrinogen interaction was significantly impaired. Notably, a similar disulfide bridge completely abrogated fibrinogen binding to alphaIIbbeta3 when alphaIIbbeta3 was activated by cytoplasmic tail truncation to mimic inside-out signaling. Thus, disruption/formation of the membrane-proximal alpha/beta stalk interface may act as an on/off switch that triggers integrin-mediated bidirectional signaling.

ANSWER 2 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-271984 [26] WPIDS

DOC. NO. NON-CPI:

N2004-215240

DOC. NO. CPI:

C2004-105664

TITLE:

Determining whether treatment of a disorder with histone deacetylase inhibitors is to be started/continued or not, using antibody capable of binding to acetylated histone

but not to deacetylated histone.

DERWENT CLASS:

B04 D16 S03

INVENTOR(S):

ARECES, L B; FARETTA, M; MACCARANA, M; MINUCCI, S;

PELICCI, P G; PICCINI, D; RONZONI, S

PATENT ASSIGNEE(S):

(GTWO-N) G2M CANCER DRUGS AG

COUNTRY COUNT:

MC MK NL PT RO SE SI SK TR

PATENT INFORMATION:

| PA' | PENT | NO   |       |    | KII | 1D I    | DAT  | Ε   | V   | VEE  | K                |               | LA | ]             | PG |    |    |    |         |    |    |    |    |
|-----|------|------|-------|----|-----|---------|------|-----|-----|------|------------------|---------------|----|---------------|----|----|----|----|---------|----|----|----|----|
| EP  | 140  | 363  | <br>9 |    | A1  | 200     | 040  | 331 | (20 | 0042 | 26) <sup>1</sup> | <br>* El      |    | <br>36        | _  |    |    |    |         |    |    |    |    |
|     | R:   | AL   | ΑT    | BE | BG  | СН      | CY   | CZ  | DE  | DK   | EE               | ES            | FΙ | FR            | GB | GR | ΙE | IT | LI      | LT | LU | LV | MC |
|     |      | MK   | NL    | PT | RO  | SE      | SI   | SK  | TR  |      |                  |               |    |               |    |    |    |    |         |    |    |    |    |
| WO  | 2004 | 1029 | 9622  | 2  | A2  | 200     | 040  | 408 | (20 | 0042 | 26)              | Eì            | 1  |               |    |    |    |    |         |    |    |    |    |
|     | RW:  | ΑT   | BE    | BG | CH  | CY      | CZ   | DE  | DK  | EΑ   | EE               | ES            | FI | FR            | GB | GH | GM | GR | HU      | ΙE | IT | KE | LS |
|     |      | LU   | MC    | MW | ΜZ  | NL      | OA   | PT  | RO  | SD   | SE               | SI            | SK | $\mathtt{SL}$ | sz | TR | TZ | ŪG | $z_{M}$ | zw |    |    |    |
|     | W:   | ΑE   | ΑG    | AL | AM  | ΑT      | ΑU   | ΑZ  | BA  | BB   | BG               | BR            | BY | BZ            | CA | CH | CN | CO | CR      | CU | CZ | DE | DK |
|     |      | DM   | DZ    | EC | EE  | EG      | ES   | FI  | GB  | GD   | GΕ               | GH            | GM | HR            | HU | ID | IL | IN | IS      | JP | KE | KG | KP |
|     |      | KR   | ΚZ    | LC | LK  | LR      | LS   | LT  | LU  | LV   | MA               | MD            | MG | MK            | MN | MW | ΜX | MZ | NI      | NO | NZ | OM | PG |
|     |      | PH   | PL    | PT | RO  | RU      | sc   | SD  | SE  | SG   | SK               | $\mathtt{SL}$ | SY | ТJ            | TM | TN | TR | TT | TZ      | UΑ | UG | US | UZ |
|     |      | VC   | VN    | YU | ZA  | $z_{M}$ | ZW   |     |     |      |                  |               |    |               |    |    |    |    |         |    |    |    |    |
| AU  | 2003 | 327  | 1663  | 3  | A1  | 200     | 0404 | 119 | (20 | 046  | 52)              |               |    |               |    |    |    |    |         |    |    |    |    |
| ΕP  | 1546 | 5712 | 2     |    | A2  | 200     | )50e | 529 | (20 | 0054 | 13)              | Eì            | 1  |               |    |    |    |    |         |    | •  |    |    |

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV

## APPLICATION DETAILS:

| PATENT NO                   | KIND     | APPLICATION                       | DATE                 |
|-----------------------------|----------|-----------------------------------|----------------------|
| EP 1403639<br>WO 2004029622 | A1<br>A2 | EP 2002-21984<br>WO 2003-EP10842  | 20020930             |
| AU 2003271663               | A1       | AU 2003-271663                    | 20030930             |
| EP 1546712                  | A2       | EP 2003-753482<br>WO 2003-EP10842 | 20030930<br>20030930 |

### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2003271663 | Al Based on | WO 2004029622 |
| EP 1546712    | A2 Based on | WO 2004029622 |

PRIORITY APPLN. INFO: EP 2002-21984

20020930

AN 2004-271984 [26] WPIDS

AB EP 1403639 A UPAB: 20040421 NOVELTY - Determining (M1) whether treatment of disorder with histone deacetylase (HDAC) inhibitor is to be started/continued/not by contacting sample from tissue affected by disorder with antibody binding to acetylated histone but not to deacetylated histone, determining histone level acetylation in sample and classifying disorder as to be treated with HDAC inhibitor when histone acetylation level is significantly less than control sample.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) use of an antibody capable of binding to acetylated histone for determining whether a treatment of a disorder with an HDAC inhibitor is to be started/continued or not, and/or the classification of tumors;
- (2) an antibody (I) capable of binding to peptides having a sequence of Ser-Gly-Arg-Gly-Lys-Gly-Lys-Gly-Leu-Gly-Lys-Gly-Gly-Ala-Lys- Arg (histone H4 tail, mono-acetylated at lysine 8) (S1) and Ser-Gly-Arg-Gly-Lys-Gly-Lys-Gly-Leu-Gly-Lys-Gly-Gly-Ala-Lys- Arg (histone H4 tail, mono-acetylated at lysine 12) (S2) but not to anyone of the peptides having the sequences of Ser-Gly-Arg-Gly-Lys-Gly-Lys-Gly-Lys-Gly-Leu-Gly-Lys-Gly-Gly-Ala-Lys- Arg (histone H4 tail, mono-acetylated at lysine 16) (S3), Ser-Gly-Arg-Gly-Lys-Gly-Gly-Lys-Gly-Leu-Gly-Lys-Gly-Gly-Ala-Lys- Arg (non-acetylated peptide) (S4), Ala-Val-Cys-Asp-Lys-Cys-Leu-Lys-Phe-Tyr-Ser-Lys and Val-Trp-Asp-Gln-Glu-Phe-Leu-Lys-Val-Asp-Gln-Gly;
- (3) an antibody (II) capable of binding to peptides having (S1), (S2) and (S3) but not to peptides having (S4);
- (4) an antibody produced by a hybridoma cell line chosen from hybridoma cell lines G2M-T25-H4ac and G2M-T52-ac deposited at DSMZ;
  - (5) a hybridoma cell line producing (I) or (II);
- (6) a hybridoma cell line which has the identifying characteristics of the cell line G2M-T25-H4ac deposited at DSMZ;
- (7) a hybridoma cell line which has the identifying characteristics of the cell line G2M-T52-ac deposited at DSMZ;
- (8) a diagnostic kit (III) for determining the level of histone acetylation containing an antibody capable of binding to acetylated histone but not to deacetylated histone, an HDAC inhibitor, and optionally, a secondary antibody directed against the antibody, and optionally reagents for the measurement of a signal derived from an antibody binding to acetylated histones; and
- (9) use of the antibodies T25 and/or T52 (IV) to direct substances conjugated to these antibodies to sites of histone hyperacetylation.
- USE (M1) is useful for determining whether a treatment of a disorder with an HDAC inhibitor is to be started/continued or not. The disorder is chosen from diseases in which the induction of hyperacetylation of histones has a beneficial effect resulting in differentiation and/or apoptosis of a patient's tumor cells, diseases that show aberrant recruitment of HDAC activity, conditions associated with abnormal gene expression, autoimmune diseases, and proliferative diseases such as skin cancer, melanoma, estrogen receptor-dependent and independent breast cancer, ovarian cancer, testosterone receptor-dependent and independent prostate cancer, renal cancer, colon and colorectal cancer, pancreatic cancer, bladder cancer, esophageal cancer, stomach cancer, genitourinary cancer, gastrointestinal cancer, uterine cancer, astrocytomas, gliomas, basal cancer and squamous cell carcinoma, sarcomas as Kaposi's sarcoma and osteosarcoma, head and neck cancer, small cell and non-small cell lung carcinoma, leukemia, lymphomas and other blood cell cancers or thyroid resistance syndrome (claimed). Dwg.0/11

L6 ANSWER 3 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN ACCESSION NUMBER: 2003-167365 [16] WPIDS

DOC. NO. CPI: C2003-043494

TITLE: Nanoparticle useful as synthetic vaccine, comprises

carrier, and ligands displayed on the carrier, where

ligands form polyvalent binding unit to produce

interaction between nanoparticle and receptors on target. B04 C06 D16

DERWENT CLASS: INVENTOR(S):

BARGATZE, R F; CUTLER, J E; GLEE, P M; HAN, Y; JUTILA, J

W; NAGY, J O; PASCUAL, D

PATENT ASSIGNEE(S):

(BARG-I) BARGATZE R F; (CUTL-I) CUTLER J E; (GLEE-I) GLEE P M; (HANY-I) HAN Y; (JUTI-I) JUTILA J W; (NAGY-I) NAGY J O; (PASC-I) PASCUAL D; (LIGO-N) LIGOCYTE PHARM INC;

(UYMO-N) UNIV MONTANA STATE-BOZEMAN

COUNTRY COUNT:

97

PATENT INFORMATION:

| PA' | TENT | NO   |      |            | KI | 4D I | OATI          | Ξ             | 1   | WEE  | K                     |          | LΑ | ]      | PG |    |    |    |    |    |    |    |    |
|-----|------|------|------|------------|----|------|---------------|---------------|-----|------|-----------------------|----------|----|--------|----|----|----|----|----|----|----|----|----|
| WO  | 200  | 2100 | 325  | <b>-</b> - | A2 | 200  | 0212          | 219           | (20 | 003  | :<br>16) <sup>;</sup> | <br>* El |    | <br>56 | -  |    |    |    |    |    |    |    |    |
|     | RW:  | ΑT   | BE   | CH         | CY | DE   | DK            | EΑ            | ES  | FI   | FR                    | GB       | GH | GM     | GR | ΙE | IT | KE | LS | LU | MC | MW | MZ |
|     |      | NL   | OA   | PT         | SD | SE   | $\mathtt{SL}$ | SZ            | TR  | TZ   | ŪĞ                    | ZW       |    |        |    |    |    |    |    |    |    |    |    |
|     | W:   | ΑE   | ΑG   | AL         | AM | ΑT   | ΑU            | ΑZ            | BA  | BB   | BG                    | BR       | BY | ΒZ     | CA | CH | CN | CO | CR | CU | CZ | DE | DK |
|     |      | DM   | DZ   | EC         | EE | ES   | FΙ            | GB            | GD  | GE   | GH                    | GM       | HR | HU     | ID | IL | IN | IS | JΡ | KE | KG | KP | KR |
|     |      | ΚZ   | LC   | LK         | LR | LS   | LT            | LU            | LV  | MA   | MD                    | MG       | MK | MN     | MW | ΜX | ΜZ | NO | NZ | PH | PL | PT | RO |
|     |      | RU   | SD   | SE         | SG | SI   | SK            | $\mathtt{SL}$ | ТJ  | TM   | TR                    | TT       | TZ | UA     | UG | US | UZ | VN | YU | ZA | ZW |    |    |
| US  | 2003 | 3223 | 3938 | 3          | A1 | 200  | 312           | 204           | (20 | 0038 | 30)                   |          |    |        |    |    |    |    |    |    |    |    |    |
| AU  | 2003 | 1297 | 7913 | 3          | A1 | 200  | 212           | 223           | (20 | 0045 | 52)                   |          |    |        |    |    |    |    |    |    |    |    |    |

### APPLICATION DETAILS:

| PATENT NO                      | KIND                 | APPLICATION                        | DATE                 |  |  |  |
|--------------------------------|----------------------|------------------------------------|----------------------|--|--|--|
| WO 2002100325<br>US 2003223938 | A2<br>Al Provisional | WO 2001-US42712<br>US 2000-239874P | 20011015             |  |  |  |
| 05 2000220000                  | Cont of              | WO 2001-US42712                    | 20011015             |  |  |  |
| AU 2001297913                  | A1                   | US 2003-412685<br>AU 2001-297913   | 20030414<br>20011015 |  |  |  |

## FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
|               |             | <del></del>   |
| AU 2001297913 | Al Based on | WO 2002100325 |

PRIORITY APPLN. INFO: US 2000-239874P 20001013; US 2003-412685 20030414

AN 2003-167365 [16] WPIDS

AB W02002100325 A UPAB: 20030307

NOVELTY - A nanoparticle (I) comprising a carrier, a first ligand (L1), and a second ligand (L2), that is different than L1, both displayed on the carrier, is new. L1 and L2 form a polyvalent binding unit to produce a specific interaction between the nanoparticle and receptor(s) on a target, and L2 interacts specifically with the receptor(s) based on its charge or hydrophobicity.

DETAILED DESCRIPTION - A nanoparticle (I) comprising a carrier, a first ligand (L1), and a second ligand (L2), that is different than L1, both displayed on the carrier, is new. L1 and L2 form a polyvalent binding unit to produce a specific interaction between the nanoparticle and receptor(s) on a target under physiologically relevant shear conditions, and L2 interacts specifically with the receptor(s) based on its charge or hydrophobicity.

INDEPENDENT CLAIMS are also included for the following:

(1) a therapeutic formulation (II) in unit dose form comprising (I), to modulate a specific interaction between a cell or toxin and its receptor on a target in a host, where L1 is derived from or mimics a

ligand on the cell or toxin;

- (2) a vaccine (III) comprising (I), where L1 is an epitope that is derived from a pathogen, pathogen-derived toxin or tumor cell, and the vaccine is formulated to elicit a protective immune response against that pathogen or tumor cell;
- (3) a diagnostic imaging agent comprising (I), and further comprising a contrast agent detectable by medical resonance imaging or other visualization techniques;
- (4) a delivery vehicle (IV) comprising (I), and an agent to be delivered to the target;
- (5) optimizing (V) a nanoparticle displaying polyvalent binding units having L1 and L2, comprises optimizing the amount of L1 on the nanoparticle under physiologically relevant shear conditions and holding the optimized amount of L1 constant, optimizing the amount of L2 under physiologically relevant shear conditions;
- (6) a nanoparticle library (VI) comprising multiple polymer beads, where each bead contains several nanoparticles associated with the surface of the polymer bead, where all of the nanoparticles associated with any one bead display the same polyvalent binding unit;
- (7) a vaccine comprising (I), and a polynucleotide sequence that encodes an epitope found on a pathogen or a tumor cell and the vaccine is formulated to elicit a protective immune response against that pathogen or tumor cell; and
  - (8) a nanoparticle produced by (VI).

ACTIVITY - Antibacterial; Fungicide; Virucide; Protozoacide; Anti-HIV; Immunostimulant; Antiinflammatory; Cytostatic.

MECHANISM OF ACTION - Vaccine; Inhibitor of lymphocyte attachment in Peyer's patch.

A variation on the Peyer's patch method was used to examine the P-selectin-mediated adhesion in a mouse mesentery venule model. A lateral incision was made into the abdominal wall to allow the small intestine to be externalized. The intestine was positioned for microscopic examination of the mesentery. A solution of PMA in phosphate buffered saline was superfused directly onto the mesentery to allow for upregulation of P-selectin in the endothelium of the mesentery venules. The area of the incision was treated and cannulation of the tail vein was performed. A variable dose of carbohydrate- and sulfate-displaying nanoparticle was administered. The results showed the reduction in number of leukocyte rolling and sticking events compared to the untreated control, and the increase in cell velocity relative to the untreated control. At the highest dosage tested (2.3 mg/kg of carbohydrate), there was a greater than 65% reduction in the number of rolling/sticking leukocytes and a nearly 90% increase in the rolling velocity, over the control.

USE -- (I) is useful for sequestration of toxins in the bloodstream of a host, by administering (I) to bind a circulating toxin or toxic metabolic product, where the first ligand is derived from or mimics a receptor that specifically binds to the toxin or toxic metabolic product. The binding is effective to produce an effect such as decreased inflammation, decreased systemic toxicity, chelation therapy, neutralization of pathogens, inhibition of metastasis, inhibition of drug intoxication, tissue regeneration, selective cellular differentiation and proliferation. (I) is also useful in a diagnostic method by allowing (I) to bind to a toxin or pathogen or an antibody against such toxins or pathogens and then detecting nanoparticles bound to such toxins, pathogen or antibodies. (III) is formulated to elicit a protective immune response against a pathogen such as Escherichia coli, Candida albicans, Brucella sp., Salmonella sp., Shigella sp., Pseudomonas sp., Bordetella sp., Clostridium sp., group B strep, E.coli 0157, Norwalk virus, anthrax, human immunodeficiency virus (HIV), sexually transmitted diseases (STDs), Chlamydia, hepatitis B virus (HBV), malaria, cell wall proteins of Candida sp., and GB3 toxin from E.coli 0157. (IV) is useful for delivering an

agent such as therapeutic or cytotoxic agent to a target. (VI) is useful for screening agents, by adding at least one candidate agent to the nanoparticle library, and detecting binding of the agent to any one or more polymer beads in the library. The candidate agent comprises a detectable label and acts as a reporter to L1. Vaccine construct comprising (I) is useful for delivering nanoparticle therapeutic molecules to an animal (all claimed).

The polymerized nanoparticle constructs and assemblies are useful as modulators, inhibitors and enhancers and drug delivery agents for a variety of interactions as well as their down-stream effects, such as pathogen-cell attachment, pathogen-derived-toxin-cell attachment, cell-cell attachment mediated diseases, integrin adhesions, complement fixation and chemokine-mediated events. The nanoparticles are readily used as synthetic vaccines.

Dwg.0/6

L6 ANSWER 5 OF 15 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-098663 [14] WPIDS

DOC. NO. CPI: C2002-030908

TITLE: Detecting heterogeneous nucleic acid sequences in

organisms and cells, useful for detecting and identifying

genetically modified organisms or their products.

DERWENT CLASS: B04 D16

INVENTOR(S): BERNAUER, H; BERNAUER, H S

PATENT ASSIGNEE(S): (BERN-I) BERNAUER H; (BERN-I) BERNAUER H S

COUNTRY COUNT: 97

PATENT INFORMATION:

| PA | rent | NO   |      |    | KII | ND I | DATI          | Ξ   | Ţ   | VEE  | K   |    | LA  | J   | PG  |    |    |    |      |     |     |       |     |
|----|------|------|------|----|-----|------|---------------|-----|-----|------|-----|----|-----|-----|-----|----|----|----|------|-----|-----|-------|-----|
|    | 100  |      |      |    |     |      |               |     | -   |      | -   |    |     | 11  | -   |    |    |    |      |     |     | ٠     |     |
| "  | RW:  |      |      |    |     |      |               |     | •   |      | •   |    |     | СМ  | GP  | TE | тт | KE | T. C | TJI | мс  | MTa7  | M7  |
|    |      |      |      |    | SD  |      |               |     |     |      |     |    | GII | Gri | GIV | 11 | 11 | KL | цэ   | цо  | PIC | 1.144 | 112 |
|    | W:   | ΑE   | AG   | AL | AM  | ΑT   | AU            | AZ  | BA  | BB   | BG  | BR | BY  | ΒZ  | CA  | СН | CN | СО | CR   | CU  | CZ  | DE    | DK  |
|    |      | DM   | DZ   | EC | EE  | ES   | FI            | GB  | GD  | GE   | GH  | GM | HR  | HU  | ID  | ΙL | IN | IS | JΡ   | KE  | KG  | KP    | KR  |
|    |      | ΚZ   | LC   | LK | LR  | LS   | LT            | LU  | LV  | MA   | MD  | MG | MK  | MN  | MW  | MX | MZ | NO | NZ   | PL  | PT  | RO    | RU  |
|    |      | SD   | SE   | SG | SI  | SK   | $\mathtt{SL}$ | ТJ  | TM  | TR   | TT  | TZ | UA  | UG  | US  | UZ | VN | YU | ZA   | zw  |     |       |     |
| ΑU | 200  | 1070 | 0545 | 5  | Α   | 200  | 0201          | L02 | (20 | 0023 | 30) |    |     |     |     |    |    |    |      |     |     |       |     |
| EP | 131  | 5834 | 4    |    | A2  | 200  | 306           | 504 | (20 | 0033 | 37) | GI | Ξ   |     |     |    |    |    |      |     |     |       |     |
|    | R:   | AL   | ΑT   | BE | CH  | CY   | DE            | DK  | ES  | FI   | FR  | GB | GR  | IE  | IT  | LI | LT | LU | LV   | MC  | MK  | NL    | PT  |

## APPLICATION DETAILS:

RO SE SI TR

| PATENT NO     | KIND | APPLICATION      | DATE     |
|---------------|------|------------------|----------|
| DE 10027218   | A1   | DE 2000-10027218 | 20000531 |
| WO 2001098533 | A2   | WO 2001-EP6198   | 20010531 |
| AU 2001070545 | Α    | AU 2001-70545    | 20010531 |
| EP 1315834    | A2   | EP 2001-949371   | 20010531 |
|               |      | WO 2001-EP6198   | 20010531 |

## FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2001070545 | A Based on  | WO 2001098533 |
| EP 1315834    | A2 Based on | WO 2001098533 |

PRIORITY APPLN. INFO: DE 2000-10027218 20000531

AN 2002-098663 [14] WPIDS

NOVELTY - Simultaneously detecting one or more heterogeneous nucleic acids (I), introduced into organisms and cells, where (I) includes at least one artificial sequence (II) that allows both determination of the identity of (I) and selective replication, and (II) are detected, and optionally identified, by hybridization to a chip and/or by sequencing, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a chip for use in the new process.

USE - The method is used (i) for detection/identification of genetically modified organisms and vectors (or their products), e.g. in foods or for detecting improper use and (ii) for correlating phenotypical features with particular regions of chromosomes.

ADVANTAGE - This method provides simple, rapid, inexpensive and unequivocal identification and detection of genetically modified organisms and vectors. (II) can be detected independently of the type of construct containing it.

Dwg.0/2

=> FIL STNGUIDE COST IN U.S. DOLLARS

FULL ESTIMATED COST

FULL ESTIMATED COST ENTRY SESSION 114.94 115.15

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jul 15, 2005 (20050715/UP).

=> fil medline biosis caplus embase wpids
COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
0.24 115.39

SINCE FILE

TOTAL

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FILE 'WPIDS' ENTERED AT 16:12:12 ON 22 JUL 2005 COPYRIGHT (C) 2005 THE THOMSON CORPORATION

=> tail and (head (s) conjugat?)
L8 113 TAIL AND (HEAD (S) CONJUGAT?)

 => t ti 110 1-11

L10 ANSWER 1 OF 11 MEDLINE on STN DUPLICATE 1

TI Protein circlets as sex pilus subunits.

L10 ANSWER 2 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

- TI Liposome useful for treating angiogenesis comprises a conjugate containing a vesicle-forming lipid and a non-biological, biomimetic antagonist, bound to its lipid bilayer.
- L10 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Crystal structure of 9-(hexadecyl)imino-4,5-diazafluorene
- L10 ANSWER 4 OF 11 MEDLINE on STN DUPLICATE 2
- TI Conjugates of synthetic cyclic peptides elicit bactericidal antibodies against a conformational epitope on a class 1 outer membrane protein of Neisseria meningitidis.
- L10 ANSWER 5 OF 11 MEDLINE on STN DUPLICATE 3
- TI Binding of metallothionein to rat spermatozoa.
- L10 ANSWER 6 OF 11 MEDLINE on STN DUPLICATE 4
- TI Relationship between fertilizing ability of frozen human spermatozoa and capacity for heparin binding and nuclear decondensation.
- L10 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN TI MEMBRANE SPECIALIZATIONS IN THE PAIRED SPERMATOZOA OF DYTISCID

WATER BEETLES.

- L10 ANSWER 8 OF 11 MEDLINE on STN DUPLICATE 5
- TI Distinct cytoskeletal domains revealed in sperm cells.
- L10 ANSWER 9 OF 11 MEDLINE on STN DUPLICATE 6
- TI The features of sperm maturation in the epididymis of a marsupial, the brushtailed possum Trichosurus vulpecula.
- L10 ANSWER 10 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
- TI The features of sperm maturation in the epididymis of a marsupial, the brushtailed possum Trichosurus vulpecula.
- L10 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Molecular probes of spermatozoan structures

# => d ibib abs 110 2,4,

L10 ANSWER 2 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-666793 [71] WPIDS

DOC. NO. CPI: C2002-187111

TITLE: Liposome useful for treating angiogenesis comprises a

conjugate containing a vesicle-forming lipid and a

non-biological, biomimetic antagonist, bound to its lipid

bilayer.

DERWENT CLASS: A96 B05 B07

INVENTOR(S): ELLENS, H M; MONCK, M A; YEH, P

PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM CORP; (ELLE-I) ELLENS H M;

(MONC-I) MONCK M A; (YEHP-I) YEH P

PATENT INFORMATION:

| PA | PENT | ИО   |      |       | KI      | ND I | DATI | 2             | 1   | WEE  | K   |    | LA | 1  | PG |    |    |    |    |    |    |    |    |
|----|------|------|------|-------|---------|------|------|---------------|-----|------|-----|----|----|----|----|----|----|----|----|----|----|----|----|
| WO | 200  | 203  | 6073 | <br>3 | <br>`A2 | 200  | 020  | <br>510       | (2) | 002  | 71) |    |    | 44 | _  |    |    |    |    |    |    |    |    |
|    | RW:  | AT   | BE   | СН    | CY      | DE   | DK   | EΑ            | ĖS  | FI   | FR  | GB | GH | GM | GR | ΙE | IT | KE | LS | LU | MC | MW | MZ |
|    |      | NL   | OA   | PT    | SD      | SE   | SL   | SZ            | TR  | TZ   | UG  | ZW |    |    |    |    |    |    |    |    |    |    |    |
|    | W:   | ΑE   | AG   | AL    | AM      | ΑT   | ΑU   | ΑZ            | BA  | BB   | BG  | BR | BY | ΒZ | CA | CH | CN | CO | CR | CU | CZ | DE | DK |
|    |      | DM   | DZ   | EC    | EE      | ES   | FI   | GB            | GD  | GE   | GH  | GM | HR | HU | ID | IL | IN | IS | JP | KE | KG | KP | KR |
|    |      | ΚZ   | LC   | LK    | LR      | LS   | LT   | LU            | LV  | MA   | MD  | MG | MK | MN | MW | MX | MZ | ИО | ΝZ | PH | PL | PT | RO |
|    |      | RU   | SD   | SE    | SG      | SI   | SK   | $\mathtt{SL}$ | ТJ  | TM   | TR  | TT | TZ | UA | UG | US | UZ | VN | ΥU | zA | ZW |    |    |
| ΑU | 2002 | 202  | 5878 | 3     | Α       | 200  | 0205 | 515           | (20 | 002  | 71) |    |    |    |    |    |    |    |    |    |    |    |    |
| ΕP | 134  | 149  | 7    |       | A2      | 200  | 0309 | 910           | (20 | 003  | 67) | E  | 1  |    |    |    |    |    |    |    |    |    |    |
|    | R:   | AL   | ΑT   | ΒE    | CH      | CY   | DÈ   | DK            | ES  | FI   | FR  | GB | GR | ΙE | IT | LI | LT | LU | LV | MC | MK | NL | PT |
|    |      | RO   | SE   | SI    | TR      |      |      |               |     |      |     |    |    |    |    |    |    |    |    |    |    |    |    |
| US | 2004 | 4013 | 3720 | )     | A1      | 200  | 0401 | L22           | (20 | 040  | 07) |    |    |    |    |    |    |    |    |    |    |    |    |
| JP | 2004 | 4512 | 2345 | 5     | W       | 200  | 0404 | 122           | (20 | 0042 | 28) |    |    | 81 |    |    |    |    |    |    |    |    |    |

### APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION     | DATE     |
|---------------|------|-----------------|----------|
| WO 2002036073 | A2   | WO 2001-US46206 | 20011029 |
| AU 2002025878 | A    | AU 2002-25878   | 20011029 |
| EP 1341497    | A2   | EP 2001-992551  | 20011029 |
|               |      | WO 2001-US46206 | 20011029 |
| US 2004013720 | A1   | WO 2001-US46206 | 20011029 |
|               |      | US 2003-415160  | 20030425 |
| JP 2004512345 | W    | WO 2001-US46206 | 20011029 |
|               |      | JP 2002-538885  | 20011029 |

# FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2002025878 | A Based on  | WO 2002036073 |
| EP 1341497    | A2 Based on | WO 2002036073 |
| JP 2004512345 | W Based on  | WO 2002036073 |

PRIORITY APPLN. INFO: US 2000-245140P 20001102; US 2003-415160 20030425

AN 2002-666793 [71] WPIDS

AB WO 200236073 A UPAB: 20030813

NOVELTY - A liposome comprises a conjugate bound to its lipid bilayer. The conjugate comprises a vesicle-forming lipid having a polar head group and a hydrophobic tail, and a non-biological, biomimetic antagonist (Al) to a receptor upregulated at a disease site, directly or indirectly chemically linked to the polar head group of the vesicle-forming lipid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) The conjugate useful for preparing a targeted liposomes; and
- (2) Use of the liposome in the manufacture of a medicament in the treatment of a disease caused by upregulation of the receptor.

ACTIVITY - Vasotropic; osteopathic; antiarthritic; anti-rheumatic; anti-diabetic; antipsoriatic; and cytostatic.

MECHANISM OF ACTION - In vitro alpha v beta 3 and alpha v beta 5 binder.

Distearaylphosphatidylethanolamine-polyethylene glycol-vitronectin receptor antagonist (DSPE-PEG-VRA) was synthesized by reacting (7-((4-amino-butyl)-(1H-benzoimidazol-2-ylmethyl)-carbamoyl)-4-methyl-3-

oxo-2,3,4,5-tetrahydro-1H-benzo(e)(1,4)diazepin-2-yl)-acetic acid (VRA) (50 mg) with DSPE-PEG-NHS in DMSO (10 ml). Excess amount of VRA (1.2 times molar excess) was used. The VRA was completely dissolved in DMSO. DSPE-PEG-NHS pre-dissolved in DMSO was added dropwise to the VRA solution. The resulting reaction mixture was stirred overnight in the dark at room temperature. The unreacted DSPE-PEG-NHS was quenched by the addition of excess glycine (5 times molar excess). The reaction mixture was diluted with 0.1M MES (morpholino ethenesulfonic acid) saline buffer (pH 5.8) and then dialyzed against the MES buffer (pH 5.8) to remove by-product, DMSO, and unreacted VRA. At this point the unreacted DSPG-PEG-NHS was hydrolyzed into DSPE-PEG-COOH. The resulting mixture was then dialyzed and lyophilized to form DSPE-PEG-VRA (VRA-lipid conjugate) (A). A liposome (L1) was tested for its binding affinity to human alpha v beta 3 or alpha v beta 5 using an in vitro solid phase binding assay described by Wong A, Hwang SM, McDevitt P, McNulty D, Stadel JM and Johanson K, studies on alpha v beta 3/ligand interaction using a (3H) SK and F-107260 binding assay (1996) Molecular pharmacology 50 (3):529 - 537. A control composition comprised cholesterol (40), PEG3400 DSPE (pegylated DSPE) (7) and POPC (53) was tested for the same binding test as that of the test conjugate. The binding affinity Ki (nm) of the test/control composition was 31/no binding effect.

USE - In the manufacture of a medicament for the treatment of diseases caused by upregulation of integrin and vitronectin receptor e.g. angiogenesis including restenosis, osteoarthritis, rheumatoid arthritis, diabetic retinopathy, hemangiomas, psoriasis and cancerous tumor (all claimed).

ADVANTAGE - The antagonist has binding affinity to the upregulation receptor, which is upregulated in the vascular endothelium of inflammation, infection or tumor sites. Dwg.0/0

L10 ANSWER 4 OF 11 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 95369902 MEDLINE DOCUMENT NUMBER: PubMed ID: 7543883

TITLE: Conjugates of synthetic cyclic peptides elicit bactericidal

antibodies against a conformational epitope on a class 1

outer membrane protein of Neisseria meningitidis.

AUTHOR: Hoogerhout P; Donders E M; van Gaans-van den Brink J A;

Kuipers B; Brugghe H F; van Unen L M; Timmermans H A; ten

Hove G J; de Jong A P; Peeters C C; +

CORPORATE SOURCE: Laboratory of Vaccine Development and Immune Mechanisms,

National Institute of Public Health and Environmental

Protection, Bilthoven, The Netherlands.

SOURCE: Infection and immunity, (1995 Sep) 63 (9) 3473-8.

Journal code: 0246127. ISSN: 0019-9567.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199509

ENTRY DATE: Entered STN: 19950930

Last Updated on STN: 19960129 Entered Medline: 19950921

AB Bactericidal antibodies directed against surface loops of class 1 outer membrane proteins play a crucial role in protection against meningitis and sepsis caused by Neisseria meningitidis. So far, all efforts to obtain protective antibodies against these apparently conformational epitopes by using linear peptide analogs have been in vain. In this study, conjugates of head-to-tail cyclic peptides encompassing the predicted top of a protective surface loop were used for immunization. A series of 18 cyclic peptides with a ring size ranging from 7 to 17 residues, conjugated to tetanus toxoid, was

investigated. Antipeptide and anti-whole-cell immunoglobulin G (IgG) titers elicited by the conjugates were determined. Conjugates of three peptides, containing 14, 15, and 17 amino acid residues (peptides 7, 12, and 13, respectively), induced an anti-whole-cell titer when Quillaja saponin A was used as the adjuvant. When alum was used as the adjuvant, the conjugate of peptide 12 did not elicit an anti-whole-cell response. From the Quillaja saponin A group, some of the sera obtained with conjugates of peptides 7 and 12 and all sera obtained with the peptide 13 conjugate were bactericidal in vitro. None of the sera evoked with alum as the adjuvant showed bactericidal activity. Nonbactericidal sera contained IgG1 primarily, whereas bactericidal sera showed significant titers of IgG2a and IgG2b. Class 1 protein-derived synthetic cyclic peptides which are capable of eliciting bactericidal antibodies, such as peptide 13 derived from meningococcal strain H44/76, represent potential candidates for a (semi)synthetic vaccine against meningococcal disease.

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154.01

=> FIL STNGUIDE

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 15:58:37 ON 22 JUL 2005

L1 10 HEAD (S) DIFFERENT (S) EPITOPE

L2 16 HEAD (S) DIFFER? (S) EPITOPE

L3 12 DUP REM L2 (4 DUPLICATES REMOVED)

L4 288 HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)

L5 26 (HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)) AND TAIL

L6 15 DUP REM L5 (11 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 16:09:56 ON 22 JUL 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 16:12:12 ON 22

L7 0 AMPHIPATHIC AND TAIL AND (HEAD (S) CONJUGAT?)

L8 113 TAIL AND (HEAD (S) CONJUGAT?)

L9 24 (BILAYER OR MEMBRANE) AND TAIL AND (HEAD (S) CONJUGAT?)

L10 11 DUP REM L9 (13 DUPLICATES REMOVED)

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=> fil medline biosis caplus embase wpids

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=> 18 not 19 L11 89 L8 NOT L9

=> dup rem 111
PROCESSING COMPLETED FOR L11
L12 75 DUP REM L11 (14 DUPLICATES REMOVED)

=> t ti 112 1-50

- L12 ANSWER 1 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

  TI Nucleic acid strand invasion to destabilize double-stranded nucleic acid hybridization comprises utilizing uracil-DNA glycosylase or an enzyme comprising a DNA N-glycosylase activity.
- L12 ANSWER 2 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

  TI Isolated or synthesized composition, useful for diagnosing and treating bladder disorders and cancer, comprises urinary bladder antiproliferative factor having sugar moieties linked to hydrophobic moiety.
- L12 ANSWER 3 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

  TI Polymeric conductive composition used to modify charge transport across nanocrystal surface, comprises functionalized head group capable of binding to nanostructure surface.
- L12 ANSWER 4 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN TI Knife bayonet.
- L12 ANSWER 5 OF 75 MEDLINE on STN DUPLICATE 1
  TI New insight into solvent effects on the formal HOO\* + HOO\* reaction.
- L12 ANSWER 6 OF 75 MEDLINE on STN DUPLICATE 2
  TI Effect of structural factors on the stability of duplexes formed by oligonucleotide conjugates with minor groove binders.
- L12 ANSWER 7 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
  TI Effect of structural factors on the stability of duplexes formed by

L12 ANSWER 8 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

- oligonucleotide conjugates with minor groove binders
- TI Organic species that facilitate charge transfer to or from nanostructures
- L12 ANSWER 9 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4 TI Combinatorial library of cyclic peptides as antibacterial agents
- L12 ANSWER 10 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

  TI Injectable liposomal composition for delivery of a water-soluble substance
  e.g. vaccine for preventing pregnancy, comprises several liposomal
  vesicles comprising a high weight ratio of lipid to encapsulated
  water-soluble substance.

- L12 ANSWER 11 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Galvanic cell, e.g. microbattery, has cathode and anode having respective vesicle comprising benzoquinone or hydroquinone, electroactive species encapsulated into the vesicles, conducting substrate, and functionalized tethers.
- L12 ANSWER 12 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Method reducing bottom resistance of artillery projectile and gear for its implementation.
- L12 ANSWER 13 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Alkyl-substituted thieno[3,2-b]thiophene polymers and their dimeric subunits
- L12 ANSWER 14 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Cobalt-catalyzed dimerization of alkenes
- L12 ANSWER 15 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- Direct observation of the ordering and molecular folding of poly[(m-phenylenevinylene) co-(2,5-dioctyloxy-p-phenylenevinylene)]
- L12 ANSWER 16 OF 75 MEDLINE on STN DUPLICATE 5
- TI A high-spin and durable polyradical: poly(4-diphenylaminium-1,2-phenylenevinylene).
- L12 ANSWER 17 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Solvatochromic, thermochromic and photoluminescent properties of poly(3-octylthiophene)
- L12 ANSWER 18 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Soft propylene resin composition for films and sheets comprises stereoblock propylene polymer containing isotactic block, and propylene-ethylene copolymer.
- L12 ANSWER 19 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Preparation of vulcanizable composition for tire tread comprises forming premix including processing aids and rubber and mixing premix with carbon black.
- L12 ANSWER 20 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Immobilization of electroactive polymerized vesicles to conducting substrate in electrode of microbattery comprises allowing suspension of vesicles to contact substrate in the presence of functionalized tether.
- L12 ANSWER 21 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- Alpha-olefin terpolymer comprises aliphatic alpha-olefins, and vinyl aromatic monomers optionally substituted by alkyl radicals, and contains block(s) of three vinyl aromatic monomers in head-tail-tail insertion fashion.
- L12 ANSWER 22 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Frolov's bullet.
- L12 ANSWER 23 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Percussive-indexing mechanism.
- L12 ANSWER 24 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Regioregular Head-to-Tail Poly(4-alkylquinoline)s: Synthesis, Characterization, Self-Organization, Photophysics, and Electroluminescence of New n-Type Conjugated Polymers

- L12 ANSWER 25 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI On the structural effects of the head-to-tail coupled oligo(3-alkylthiophenes) on their optical properties
- L12 ANSWER 26 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Generating a modified protein with reduced antigenicity for treating cancer, AIDS, autoimmune diseases, comprises identifying a protein region antigenic in the first subject using antiserum from either the first or a second subject.
- L12 ANSWER 27 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New n-type polythiophene composition for fabricating thin film field effect transistors.
- L12 ANSWER 28 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Bullet of sporting gun cartridge for rifled weapon.
- L12 ANSWER 29 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Poly(1,2-phenylenevinylene) Ferromagnetically 3,5-Bearing Phenoxyl Radicals
- L12 ANSWER 30 OF 75 MEDLINE on STN DUPLICATE 6
- TI Design and synthesis of a 256-membered pi-conjugated oligomer library of regionegular head-to-tail coupled quater(3-arylthiophene)s.
- L12 ANSWER 31 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
- TI Epitopes formed by non-covalent association of conjugates
- L12 ANSWER 32 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Sequence Length Distributions (Microstructure) of Regionegular Poly(3-alkylthiophene)s and Related Conjugated Polymers and Their Use in Simulating  $\pi-\pi^*$  Absorption Peak Profiles
- L12 ANSWER 33 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Poly(3-phenylgalvinoxylthiophene). A new conjugated polyradical with high spin concentration
- L12 ANSWER 34 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Undular jump in open-channel flow over a sill
- L12 ANSWER 35 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Preparation and characterization of regionegular head-totail  $\pi$ - conjugated poly(pyridine-2,5-diyl)s
- L12 ANSWER 36 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Use of asialo-glycoproteins for treating liver disease, e.g. viral hepatitis, and targeting a glycoprotein to a hepatocyte.
- L12 ANSWER 37 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Grinding head.
- L12 ANSWER 38 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Copolymer of aromatic vinyl, olefin, and non-conjugated diene having improved mechanical strength, elasticity and transparency.
- L12 ANSWER 39 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Ferromagnetic Spin Alignment in Head-to-Tail Coupled Oligo(1,4-phenyleneethynylene)s and Oligo(1,4-phenylenevinylene)s Bearing Pendant p-Phenylenediamine Radical Cations
- L12 ANSWER 40 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN

- TI Two-dimensional crystals of poly(3-alkylthiophene)s: direct visualization of polymer folds in submolecular resolution
- L12 ANSWER 41 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Preparation of Conjugated Gels of Regioregular HT Sexi(3-n-octylthiophene) and Related Star Molecules
- L12 ANSWER 42 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI  $\pi$ -Conjugated polymers prepared by organometallic polycondensation and metal complexes of the polymers
- L12 ANSWER 43 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Regioregular polymerization of 3-semifluoroalkylthiophenes.
- L12 ANSWER 44 OF 75 MEDLINE on STN DUPLICATE 8
- TI Synthesis of a single-tailed cationic lipid and investigation of its transfection.
- L12 ANSWER 45 OF 75 MEDLINE on STN DUPLICATE 9
- TI The Xenopus Emx genes identify presumptive dorsal telencephalon and are induced by head organizer signals.
- L12 ANSWER 46 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Lubricating oil for mitigating sludge formation in engine oil contains a minor amount of alkyl substituted hydroxy aromatic compound formed by alkylation of ethylene -alpha-olefin copolymer.
- L12 ANSWER 47 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Synthesis and characterization of poly[3-(butylthio)thiophene]: a regioregular head-to-tail polymer
- L12 ANSWER 48 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Use of nucleic acid ligands in flow cytometry
- L12 ANSWER 49 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10
- TI Living Polymerization of (o-(Trimethylsilyl)phenyl)acetylene by Molybdenum Imido Alkylidene Complexes
- L12 ANSWER 50 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Solvent effect on the bathochromic shifts of push-pull dihexylbithiophenes with head-to-head and head-to-tail orientations
- => t ti 112 51-75
- L12 ANSWER 51 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Electroluminescence of regionegular poly(alkylthiophenes)
- L12 ANSWER 52 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Thiophene:alkylthiophene copolymers from substituted dialkyloligothiophenes
- L12 ANSWER 53 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI A dramatic conjugational interchange in the regionegular polythiophene, HT-poly(3-[2,5,8-trioxanonyl]thiophene) via a chemoselective recognition response
- L12 ANSWER 54 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Mercurophilic 1-(8,8-dicyanoheptafulven-3-yl)aza-15-crown-5 ether. Synthesis, x-ray structural analysis, and fixation of its derivative on a polymer

- L12 ANSWER 55 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI The effect of stereoregularity on the structure of poly(octylthiophene): an x-ray diffraction study
- L12 ANSWER 56 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Site-specific immunoconjugates
- L12 ANSWER 57 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Conducting polymers from anodic coupling of some regiochemically defined dialkoxy-substituted thiophene oligomers
- L12 ANSWER 58 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI The tuning of conjugation by recipe: the synthesis and properties of random head-to-tail poly(3-alkylthiophene) copolymers
- L12 ANSWER 59 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- Polymeric nonlinear optical material contains functional gps. at both ends which can form hydrogen bond in head-to-tail form, and does not cause relaxation or orientation.
- L12 ANSWER 60 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Synthesis and physical properties of self-orienting head-to-tail polythiophenes
- L12 ANSWER 61 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Toward tuning electrical and optical properties in conjugated polymers using side-chains: highly conductive head-to-tail, heteroatom functionalized polythiophenes
- L12 ANSWER 62 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Low-temperature magnetic properties for poly(3-alkylthiophenes) and poly(4,4'-dialkyl-2,2'-bithiophenes)
- L12 ANSWER 63 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- Polyazomethine conjugated polymer film with second-order nonlinear optical properties fabricated by electric-field-assisted chemical vapor deposition
- L12 ANSWER 64 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Reactions proceeding via the reactive intermediate  $\alpha\text{-vinyl-p-}$  xylylene. Contrasting orientations in the formation of cyclic dimers and polymer
- L12 ANSWER 65 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Structural and quantitative analysis of surface modified poly(vinylidene fluoride) films using ATR FT-IR spectroscopy
- L12 ANSWER 66 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Variable teeth angle reamer has calibrating section with land widening from head to tail end while front angle of teeth decreases.
- L12 ANSWER 67 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Improving colour of aromatic thermoplastic polymer by treatment with peroxy cpd..
- L12 ANSWER 68 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI The Michael induced Ramberg-Baecklund homologation to conjugated isoprenoids
- L12 ANSWER 69 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Electroinitiated polymerization through acetylene and nitrile group bonds

- L12 ANSWER 70 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Thermal and radiation-induced dehydrochlorination of poly(vinyl chloride). II. Head-to-head structures
- L12 ANSWER 71 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Structure and stereochemistry of nucleic acid components and their reaction products. III. Crystal structure of the potassium salt of N-(purin-6-ylcarbamoyl)-L-threonine. Possible role of hypermodified bases adjacent to anticodon in codon-anticodon interaction
- L12 ANSWER 72 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Polymer microstructure
- L12 ANSWER 73 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- II Molecular-orbital theory of reactivity in radical polymerization. II
- L12 ANSWER 74 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Long-chain acids. I. Extension of the isoprene rule
- L12 ANSWER 75 OF 75 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Cordless tyre with tread of ethylene/propylene/diene terpolymer, and sidewall of segmented copolyester.

=> d ibib abs 112 44,48,56

L12 ANSWER 44 OF 75 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 1999459173 MEDLINE DOCUMENT NUMBER: PubMed ID: 10528072

TITLE: Synthesis of a single-tailed cationic lipid and

investigation of its transfection.

AUTHOR: Tang F; Hughes J A

CORPORATE SOURCE: University of Florida, College of Pharmacy, Department of

Pharmaceutics, Gainesville, FL 32610, USA.

CONTRACT NUMBER: PO1-AG10485 (NIA)

R29-H 1 55779

SOURCE: Journal of controlled release : official journal of the

Controlled Release Society, (1999 Dec 6) 62 (3) 345-58.

Journal code: 8607908. ISSN: 0168-3659.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199912

ENTRY DATE: Entered STN: 20000113

Last Updated on STN: 20000113 Entered Medline: 19991216

Single-tailed cationic lipids were originally reported to have low AB transfection efficiency and high toxicity in plasmid delivery. We hypothesized that particular single-tailed cationic lipids may also function in plasmid transfection. To test this hypothesis, we synthesized a new cationic lipid-oleoyl ornithinate (OLON). To decrease cytotoxicity, we then introduced a potential biodegradable ester bond in the tail of lipid yielding 6-lauroxyhexyl ornithinate (LHON). The data demonstrated that the cytotoxicity of LHON was lower than that of 1,2-dioleoy1-3-trimethylammonium-propane (DOTAP) or OLON. To investigate the transfection activity of the new lipids and determine the cellular uptake of DNA/liposome complexes, we compared the transfection of liposomes produced from double-tailed 1',2'-dioleyl-sn-glycero-3'-succinyl-1, 6-hexanediol ornithine conjugate (DOGSHDO) with an ornithine headgroup, single-tailed OLON with an ornithine head group, double-tailed DOTAP with quaternary amine group, and single-tailed

cetyltrimethylammonium bromide (CTAB) with a quaternary amine group. At the optimal ratios as defined in transfection experiments, OLON/DOPE had more than 10 times the transgene expression than other liposomes even though the DNA uptake was not necessarily greater. In the experiments comparing the release of DNA from DNA/liposome complexes by anionic substances, a greater fraction of DNA was released from DNA/OLON/DOPE complexes than that from DNA/DOTAP/DOPE complexes.

L12 ANSWER 48 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:145215 CAPLUS

DOCUMENT NUMBER: 126:141764

TITLE: Use of nucleic acid ligands in flow cytometry

INVENTOR(S): Davis, Ken; Jayasena, Sumedha; Gold, Larry

PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA; Becton Dickinson

and Company

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 127

PATENT INFORMATION:

|         | TENT          |     |      |     |     |     | DATE |      |     |      |       |       |     |     | ľ    | DATE      |     |
|---------|---------------|-----|------|-----|-----|-----|------|------|-----|------|-------|-------|-----|-----|------|-----------|-----|
|         | 9641          |     |      |     |     |     |      |      |     |      | 996-1 |       |     |     | 1    | <br>19960 | 530 |
|         |               |     |      |     |     |     |      |      |     |      |       |       |     |     |      | DK,       |     |
|         |               | ES, | FΙ,  | GB, | GE, | HU, | IS,  | JP,  | KE, | KG,  | KP,   | KR,   | ΚZ, | LK, | LR,  | LS,       | LT, |
|         |               | LU, | LV,  | MD, | MG, | MK, | MN,  | MW,  | MX, | NO,  | NZ,   | PL,   | PT, | RO, | RU,  | SD,       | SE, |
|         |               | SG, | SI   |     |     |     |      |      |     |      |       |       |     |     |      |           |     |
|         | RW:           | ΚE, | LS,  | MW, | SD, | SZ, | UG,  | AT,  | BE, | CH,  | DE,   | DK,   | ES, | FI, | FR,  | GB,       | GR, |
|         |               |     |      |     |     |     |      |      |     |      |       |       |     |     |      | GN,       |     |
| US      | 5853          | 984 |      |     | Α   |     | 1998 | 1229 | J.  | US 1 | 995-4 | 47972 | 29  |     | 1    | 9950      | 607 |
| AU      | 9661          | 470 |      |     | A1  |     | 1996 | 1230 | 1   | AU 1 | 996-6 | 61470 | 0   |     | 1    | .9960     | 530 |
| EP      | 8322          | 99  |      |     | A1  |     | 1998 | 0410 | ]   | EP 1 | 996-9 | 9190  | 17  |     | 1    | .9960     | 530 |
|         | R:            | ΑT, | BE,  | CH, | DE, | DK, | ES,  | FR,  | GB, | GR,  | IT,   | LI,   | LU, | NL, | SE,  | MC,       | PT, |
|         |               | ΙE, |      |     |     |     |      |      |     |      |       |       |     |     |      |           |     |
|         | 7737          |     |      |     | B2  |     | 2004 | 0603 | 1   | AU 2 | 001-3 | 1825  | 7   |     | 2    | 0010      | 202 |
| AU      | 7738<br>Y APP | 15  |      |     | В2  |     | 2004 | 0610 | 1   | AU 2 | 001-2 | 29834 | 4   |     | 2    | 0010      | 323 |
| PRIORIT | Y APP         | LN. | INFO | .:  |     |     |      |      | Ţ   | JS 1 | 995-4 | 17972 | 29  | I   | 1    | 9950      | 607 |
|         |               |     |      |     |     |     |      |      | Ţ   | JS 1 | 990-5 | 53642 | 28  | E   | 32 1 | 9900      | 611 |
|         |               |     |      |     |     |     |      |      | 7   | AU 1 | 991-8 | 3206  | l   | F   | AO 1 | 9910      | 610 |
|         |               |     |      |     |     |     |      |      | Ţ   | JS 1 | 991-7 | 71413 | 31  | P   | 12 1 | 9910      | 610 |
|         |               |     |      |     |     |     |      |      | Ţ   | JS 1 | 992-9 | 96462 | 24  | P   | 12 1 | 9921      | 021 |
|         |               |     |      |     |     |     |      |      | Ţ   | JS 1 | 994-1 | L995( | 07  | · P | 12 1 | 9940      | 222 |
|         |               |     |      |     |     |     |      |      |     |      |       |       |     |     | 12 1 | 9940      | 428 |
|         |               |     |      |     |     |     |      |      | 1   | AU 1 | 996-5 | 8839  | 9   | 7   | 13 1 | 9960      | 530 |
|         |               |     |      |     |     |     |      |      | V   | WO 1 | 996–ા | JS808 | 39  | W   | 7 1  | 9960      | 530 |
|         |               |     |      |     |     |     |      |      | 1   | AU 1 | 996-6 | 51611 | L   | P   | 13 1 | 9960      | 604 |

AB This invention discloses the use of SELEX-developed high-affinity oligonucleotide ligands in flow cytometry diagnostic applications. Specifically, DNA ligands having one or more fluorophore mols. attached are disclosed which are useful in flow cytometry.

L12 ANSWER 56 OF 75 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:83878 CAPLUS

DOCUMENT NUMBER: 124:172723

TITLE: Site-specific immunoconjugates

AUTHOR(S): Werlen, R. C.; Lankinen, M.; Smith, A.; Chernushevich,

I.; Standing, K. G.; Blakey, D. C.; Shuttleworth, H.;

Melton, R. G.; Offord, R. E.; Rose, K.

CORPORATE SOURCE: Dep. Biochim. Med., Centre Med. Univ., Geneca,

CH-1211, Switz.

SOURCE: Tumor Targeting (1995), 1(5), 251-8

CODEN: TUTAF9; ISSN: 1351-8488

PUBLISHER: Chapman & Hall

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review and discussion with 19 refs. The conjugation of two proteins with different activities in order to get a conjugate with a new hybrid activity is a field of intense investigation. The standard way of preparing such

conjugates uses random acylation of lysine side-chains with heterobifunctional reagents, leading to a mixture of conjugates where both protein partners are linked to one another in different orientations. To circumvent this difficulty, we are developing precise conjugation techniques for the preparation of site-specific protein conjugates. Here we review the preparation, characterization and the use of three such site-specific immunoconjugates: an antibody fragment-enzyme conjugate designed for ADEPT (antibody-directed enzyme prodrug therapy) and two F(ab')3 constructions prepared with different linkers. The ADEPT conjugate is a head-to-tail conjugate between an F(ab')3 antibody fragment and the enzyme carboxypeptidase G2 (CPG2). The components are linked through the formation of a hydrazone bond between a carbohydrazide, introduced at the C-terminus of the truncated heavy chain of the antibody fragment by reverse proteolysis, and an aldehyde, obtained by mild periodate oxidation of a threonine introduced at the N-terminus of the CPG2 by genetic engineering. This conjugate has been characterized by ESI-TOF (electrospray ionization time of flight) mass spectrometry and its in vitro and in vivo behavior was compared with that of a corresponding random conjugate. For the preparation of both F(ab')3 constructions, an Fab with a single thiol group was first prepared by

digestion with appropriate proteases. In the first case, the thiol was then converted to an aminooxy group. A trivalent construct was then obtained by polyoxime formation with a trialdehyde template. This F(ab')3 has been characterized by ESI-TOF mass spectrometry and its biodistribution in tumor-bearing mice has been investigated. The second F(ab')3 was obtained starting with the same Fab, but the trivalent construct was prepared on a template containing two aldehydes and a maleimide group, allowing the introduction of three Fab in three different steps.

## => d his

(FILE 'HOME' ENTERED AT 15:58:16 ON 22 JUL 2005)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 15:58:37 ON 22 JUL 2005

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L1 10 HEAD (S) DIFFERENT (S) EPITOPE
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FILE 'STNGUIDE' ENTERED AT 16:09:56 ON 22 JUL 2005

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 16:12:12 ON 22 JUL 2005

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L7 0 AMPHIPATHIC AND TAIL AND (HEAD (S) CONJUGAT?)
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FILE 'STNGUIDE' ENTERED AT 16:16:53 ON 22 JUL 2005

L2 16 HEAD (S) DIFFER? (S) EPITOPE

L3 12 DUP REM L2 (4 DUPLICATES REMOVED)

L4 288 HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)

L5 26 (HEAD (S) DIFFER? (S) (LIGAND OR RECEPTOR)) AND TAIL

L6 15 DUP REM L5 (11 DUPLICATES REMOVED)

L8 113 TAIL AND (HEAD (S) CONJUGAT?)

L9 24 (BILAYER OR MEMBRANE) AND TAIL AND (HEAD (S) CONJUGAT?)

L10 11 DUP REM L9 (13 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 16:24:09 ON 22 JUL 2005

L11 89 L8 NOT L9

L12 75 DUP REM L11 (14 DUPLICATES REMOVED)

=> (bilayer or membrane) and (head (s) conjugat?)

L13 87 (BILAYER OR MEMBRANE) AND (HEAD (S) CONJUGAT?)

=> 113 not 19

L14 63 L13 NOT L9

=> dup rem 114

PROCESSING COMPLETED FOR L14

L15 38 DUP REM L14 (25 DUPLICATES REMOVED)

=> t ti 115 1-38

- L15 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Formulations, conjugates, and combinations of drugs for the treatment of neoplasms
- L15 ANSWER 2 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New anti-tumor and cobalamin conjugate comprising cobalamin or its derivatives or analogue, linker and anti-tumor drug to treat tumor related disorder or disease e.g. Hodgkin's disease, neurofibromatosis and cervical dysplasia.
- L15 ANSWER 3 OF 38 MEDLINE on STN DUPLICATE 1
- TI Preferred conformations of endogenous cannabinoid ligand anandamide.
- L15 ANSWER 4 OF 38 MEDLINE on STN DUPLICATE 2
- TI In vivo and in vitro reconstitution of atg8 conjugation essential for autophagy.
- L15 ANSWER 5 OF 38 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
- TI Macaque sperm release ESP13.2 and PSP94 during capacitation: The absence of ESP13.2 is linked to sperm-zona recognition and binding.
- L15 ANSWER 6 OF 38 MEDLINE on STN DUPLICATE 3
- TI Distal cationic poly(ethylene glycol) lipid conjugates in large unilamellar vesicles prepared by extrusion enhance liposomal cellular uptake.
- L15 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
- TI Human monoclonal antibodies specific to prostate specific membrane antigen (PSMA) for cancer diagnosis and therapy
- L15 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Humanized murine anti-epithelial glycoprotein 1 (EGP-1) antibodies RS7 and conjugates for diagnosis and treatment of cancer
- L15 ANSWER 9 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Enhancement of transport of biological agent, e.g. antifungal agent, across membrane, comprising use of conjugate containing biological agent and oligomer with guanidino or amidino side chains.
- L15 ANSWER 10 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New colloidal carrier composition useful for e.g. passive targeting of drugs to sites of pathology, comprises active agent and lipid-polymer conjugate comprising amphiphilic lipid and polymer e.g. poly-(amino acid

derivative).

- L15 ANSWER 11 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New lipid polymer conjugate useful for e.g. vesicular **bilayer** systems for use e.g. in therapy, comprises e.g. poly-amino acid derivative or poly-amino acid analogue polymer, and lipid attached to nitrogen or carbon terminal of polymer.
- L15 ANSWER 12 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New isolated or recombinant Bcl-B nucleic acids and polypeptides, for treating a disorder associated with apoptosis, such as cell degenerative or proliferative disorder e.g. cancer, Alzheimer's disease or Parkinson's disease.
- L15 ANSWER 13 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Biocompatible material useful for e.g. controlling cellular growth comprises at least two component surface.
- L15 ANSWER 14 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Composition comprising a combination of an oxidizing and/or reducing agent, a protein-denaturing agent, and a hapten, useful for treating neoplasms, tumors, and cancers.
- L15 ANSWER 15 OF 38 MEDLINE on STN
- TI Orienting otolith-ocular reflexes in the rabbit during static and dynamic tilts and off-vertical axis rotation.
- L15 ANSWER 16 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI New membrane permanent peptide complexes for medical imaging, diagnostics and therapy.
- L15 ANSWER 17 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Polymeric assay film for direct colorimetric detection of small molecules such as pathogens.
- L15 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Effect of PEG-lipid conjugates on the phase behavior of phosphatidylethanolamine dispersions
- L15 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Receptor membranes.
- L15 ANSWER 20 OF 38 MEDLINE on STN
- TI Otolith and semicircular canal contributions to the human binocular response to roll oscillation.
- L15 ANSWER 21 OF 38 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 5
- TI Determination of imazethapyr using capillary column flow injection liposome immunoanalysis.
- L15 ANSWER 22 OF 38 MEDLINE on STN
- TI Lectin binding characteristics of squamous cell carcinomas of the head and neck.
- L15 ANSWER 23 OF 38 MEDLINE on STN DUPLICATE 6
- TI Evidence for a direct action of GH on haemopoietic cells of a marine fish, the gilthead sea bream (Sparus aurata).
- L15 ANSWER 24 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Ink-jet recording **head** with uniform **conjugation** of the second.

- L15 ANSWER 25 OF 38 MEDLINE on STN DUPLICATE 7
- TI Lipid-amphotericin B complex structure in solution: a possible first step in the aggregation process in cell membranes.
- L15 ANSWER 26 OF 38 MEDLINE on STN
- TI [Clinical evaluation of otolithic function by the measurement of ocular cyclotorsion and skew deviation].

  Evaluation clinique de la fonction otolithique par mesure de la cyclotorsion oculaire et de la "skew deviation".
- L15 ANSWER 27 OF 38 MEDLINE on STN DUPLICATE 8
- TI Induction of vesicle-to-micelle transition by bile salts for DOPE vesicles incorporating immunoglobulin G.
- L15 ANSWER 28 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
- TI Receptor membrane for bio-sensors comprising a closely packed array of self-assembling amphiphilic molecules having ion channels and/or receptor molecules.
- L15 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Differential localization of glycoconjugates having affinity for concanavalin A on the surface of the sperm head in the testis, the epididymis, and the ejaculate of the ram
- L15 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI pH-dependent stability and fusion of liposomes combining protonatable double-chain amphiphiles with phosphatidylethanolamine
- L15 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Identifying regions of membrane proteins in contact with phospholipid head groups: covalent attachment of a new class of aldehyde lipid labels to cytochrome c oxidase
- L15 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
- TI Localization of carbohydrate components in human synovial lining cells by binding with fluoresceinated lectins and their digestion with neuraminidase
- L15 ANSWER 33 OF 38 MEDLINE on STN DUPLICATE 9
- TI Immunocytochemical localization of acrosin in boar spermatozoa.
- L15 ANSWER 34 OF 38 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
- TI Immunocytochemical localization of acrosin in boar spermatozoa.
- L15 ANSWER 35 OF 38 MEDLINE on STN
- TI Branching pattern and properties of vertical- and horizontal-related excitatory vestibuloocular neurons in the cat.
- L15 ANSWER 36 OF 38 MEDLINE on STN DUPLICATE 10
- TI A novel approach for the topographical localization of glycolipids on the cell surface.
- L15 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 11
- TI Physiological studies on the sperm surface component responsible for sperm-egg bonding in sea urchin fertilization. II. Effect of concanavalin A on the fertilizing capacity of sperm
- L15 ANSWER 38 OF 38 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
- TI Ultrasonic tomography in obstetrics and gynecology: Experimental results

=> d ibib abs 1,9-11,13-15,17-19,25,27-31,36 115

L15 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:216611 CAPLUS

DOCUMENT NUMBER: 142:291340

TITLE: Formulations, conjugates, and combinations of drugs

for the treatment of neoplasms

INVENTOR(S): Nichols, James M.; Foley, Michael A.; Keith, Curtis;

Padval, Mahesh; Elliott, Peter Combinatorx, Incorporated, USA

PATENT ASSIGNEE(S): Combinatorx, Incorporated, SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| ]     | PATENT 1 | NO.   |      |     | KIN  | D   | DATE  |       |     | APPL  | ICAT: | ION I | .00     |              | D.   | ATE   |     |
|-------|----------|-------|------|-----|------|-----|-------|-------|-----|-------|-------|-------|---------|--------------|------|-------|-----|
| ,     | WO 2005  | 0209  | 13   |     | A2   | _   | 2005  | 0310  | Ī   | WO 2  | 004-1 | JS27  | <br>695 | <del>-</del> | 2    | 0040  | 825 |
|       | W:       |       |      |     |      |     | AU,   |       |     |       |       |       |         |              |      |       |     |
|       |          | CN,   | CO,  | CR, | CU,  | CZ, | DE,   | DK,   | DM, | DZ,   | EC,   | EE,   | EG,     | ES,          | FI,  | GB,   | GD, |
|       |          | GE,   | GH,  | GM, | HR,  | HU, | ID,   | IL,   | IN, | IS,   | JP,   | KE,   | KG,     | KP,          | KR,  | KZ,   | LC, |
|       |          | LK,   | LR,  | LS, | LT,  | LU, | LV,   | MA,   | MD, | MG,   | MK,   | MN,   | MW,     | MX,          | MZ,  | NA,   | NI, |
|       |          | NO,   | NZ,  | OM, | PG,  | PH, | PL,   | PT,   | RO, | RU,   | SC,   | SD,   | SE,     | SG,          | SK,  | SL,   | SY, |
|       |          | ТJ,   | TM,  | TN, | TR,  | TT, | TZ,   | UA,   | UG, | US,   | UZ,   | VC,   | VN,     | YU,          | ZA,  | ZM,   | ZW  |
|       | RW:      | BW,   | GH,  | GM, | KE,  | LS, | MW,   | MZ,   | NA, | SD,   | SL,   | SZ,   | TZ,     | UG,          | ZM,  | ZW,   | AM, |
|       |          | ΑZ,   | BY,  | KG, | ΚZ,  | MD, | RU,   | ТJ,   | TM, | ΑT,   | BE,   | BG,   | CH,     | CY,          | CZ,  | DE,   | DK, |
|       |          | EE,   | ES,  | FI, | FR,  | GB, | GR,   | HU,   | ΙE, | IT,   | LU,   | MC,   | NL,     | PL,          | PT,  | RO,   | SE, |
|       |          | SI,   | SK,  | TR, | BF,  | ВJ, | CF,   | CG,   | CI, | CM,   | GΑ,   | GN,   | GQ,     | GW,          | ML,  | MR,   | NE, |
|       |          | SN,   | TD,  | TG  |      |     |       |       |     |       |       |       |         |              |      |       |     |
| τ     | JS 2005  | 0800. | 75   |     | A1   |     | 2005  | 0414  | Į   | JS 20 | 004-9 | 92583 | 35      |              | 20   | 00408 | 325 |
| PRIOR | ITY APP  | LN.   | INFO | .:  |      |     |       |       | Ţ   | JS 20 | 003-4 | 1976: | L7P     | i            | P 20 | 00308 | 325 |
| OTHER | SOURCE   | (S):  |      |     | MARI | PAT | 142:2 | 29134 | 40  |       |       |       |         |              |      |       |     |

PRIORITY APPLN. INFO.:

US 2003-497617P P 20030825

OTHER SOURCE(S):

MARPAT 142:291340

AB The invention provides formulations and structural modifications for phenothiazine compds, which result in altered biodistribution thereby

phenothiazine compds. which result in altered biodistribution, thereby reducing the occurrence of adverse reactions associated with this class of drug.

L15 ANSWER 9 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-558976 [52] WPIDS

DOC. NO. CPI: C2003-150616

TITLE: Enhancement of transport of biological agent, e.g.

antifungal agent, across membrane, comprising

use of conjugate containing biological agent and oligomer

with guanidino or amidino side chains.

DERWENT CLASS: B05

INVENTOR(S): JESSOP, T C; PATTABIRAMAN, K; PELKEY, E T; ROTHBARD, J B;

WENDER, P A

PATENT ASSIGNEE(S): (JESS-I) JESSOP T C; (PATT-I) PATTABIRAMAN K; (PELK-I)

PELKEY E T; (ROTH-I) ROTHBARD J B; (WEND-I) WENDER P A;

(CELL-N) CELLGATE INC; (STRD) UNIV LELAND STANFORD JUNIOR

COUNTRY COUNT: 103

PATENT INFORMATION:

| PATENT NO | KIND DATE | WEEK | LΑ | PG |
|-----------|-----------|------|----|----|
|           |           |      |    |    |

WO 2003049772 A2 20030619 (200352)\* EN 58

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU

```
MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA
ZM ZW

US 2003185788 A1 20031002 (200365)
AU 2002359679 A1 20030623 (200420)
US 2004161405 A9 20040819 (200455)
EP 1461084 A2 20040929 (200463) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC
```

#### APPLICATION DETAILS:

| PATENT NO     | KIND           | APPLICATION     | DATE     |
|---------------|----------------|-----------------|----------|
| WO 2003049772 | A2             | WO 2002-US39698 | 20021211 |
| US 2003185788 | Al Provisional | US 2001-339696P | 20011211 |
|               |                | US 2002-318278  | 20021211 |
| AU 2002359679 | A1             | AU 2002-359679  | 20021211 |
| US 2004161405 | A9 Provisional | US 2001-339696P | 20011211 |
|               |                | US 2002-318278  | 20021211 |
| EP 1461084    | A2             | EP 2002-794232  | 20021211 |
|               |                | WO 2002-US39698 | 20021211 |

#### FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| AU 2002359679 | Al Based on | WO 2003049772 |
| EP 1461084    | A2 Based on | WO 2003049772 |

PRIORITY APPLN. INFO: US 2001-339696P 20011211; US 2002-318278 20021211

MK NL PT RO SE SI SK TR

AN 2003-558976 [52] WPIDS AB W02003049772 A UPAB: 2003

WO2003049772 A UPAB: 20030813

NOVELTY - The transport of a compound across a biological membrane is enhanced by contacting the membrane with a conjugate containing the biological agent covalently attached to a transport reagent containing a polymer with comprising 6 - 25 subunits with a guanidino or amidino side chain moiety in at least 50% of the subunits.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for guanidinium compounds of formula (I). m=6-25;

T = first terminal functional group or L (both optionally
protected);

L = linking group having an attached therapeutic agent;

W = second terminal functional group or L (both optionally protected);

Xi = backbone subunit;

i = numbering system of 1 - 25;

Yi = H, amino acid side chain, (hetero)aryl, 1-8C alkylene, 2-8C alkenylene, 2-8C alkynylene, 2-8C heteroalkylene, 3-8C cycloalkylalkylene, 2-8C spirocycloalkylene and/or (hetero)arylene; n = 0 - 2;

Zi = -NHC(=NH2)NH2(+), pyrrolidine-1-carboxamidin-yl, 2-amino-4,5-dihydro-3H-imidazol-1-ium-5-yl, imidazolidin-2-ylidene-ammonium-1-yl, 1,3-dihydro-benzoimidazol-2-ylidene-ammonium-1-yl, 1,3-dihydro-imidazol-2-ylidene-ammonium-1-yl, or 1,3-dihydro-benzoimidazol-2-ylidene-ammonium-yl; and provided that:

- (i) when n is 0, then Yi is H, amino acid side chain, or (hetero)aryl;
- (ii) when n is 1, then Yi is 1-8C alkylene, 2-8C alkenylene, 2-8C alkynylene, 2-8C heteroalkylene, 3-8C cycloalkylalkylene, 2-8C spirocycloalkylene and/or (hetero)arylene;
- (iii) T and W do not simultaneously contain an attached therapeutic agent; and  $\ensuremath{\text{\textbf{w}}}$
- (iv) (I) has at least 4 guanidinium moieties and the position of the compound joining W and T is not a polypeptide.

USE - For enhancing transport of biological agents such as diagnostic agent, anticancer agent, antifungal agent, antibacterial agent or anti-inflammation agent, across a biological membrane (claimed). The method is also useful for screening the biological activity of agents which are unable or poorly able to enter cells by themselves.

ADVANTAGE - The method promotes transport of the conjugate across the membrane at a higher rate than the trans-membrane transport rate of the biological agent in the non-conjugated form. It provides an efficient way of identifying active agents that might not otherwise be accessible through large scale screening programs, for lack of an effective and convenient way of transporting the agent into the cell or organelle, and enables the testing of activities of agents that by themselves are unable or poorly able to enter cells to manifest biological activity. The delivery of small organic molecules having poor solubilities in aqueous liquids such as serum and aqueous saline can be administered in greater dosage and with more efficacy.

Dwg.0/23

L15 ANSWER 10 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-229291 [22] WPIDS

CROSS REFERENCE: 2003-247851 [24] DOC. NO. CPI: C2003-058853

TITLE: New colloidal carrier composition useful for e.g. passive

targeting of drugs to sites of pathology, comprises active agent and lipid-polymer conjugate comprising amphiphilic lipid and polymer e.g. poly-(amino acid

derivative).

DERWENT CLASS: A23 A96 B07

INVENTOR(S): BRUIN, P; DE BOER, L W T; DE VRINGER, T; HENNINK, W E;

METSELAAR, J M; OUSSOREN, C; STORM, G; DEBOER, L W T;

HENNICK, W E; THEODORUS, D B L W

PATENT ASSIGNEE(S): (YAMA) YAMANOUCHI EURO BV; (BRUI-I) BRUIN P; (DVRI-I) DE

VRINGER T; (HENN-I) HENNICK W E; (METS-I) METSELAAR J M; (OUSS-I) OUSSOREN C; (STOR-I) STORM G; (THEO-I) THEODORUS

DBLW

91

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2002098952 Al 20021212 (200322)\* EN 51

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AU BA BB BG BR BZ CA CN CO CR CU CZ DM DZ EC EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ OM PH PL RO SG SI SK TT UA US UZ VN YU ZA

EP 1392755 A1 20040303 (200417) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR ,

NO 2003005264 A 20040128 (200419)

SK 2003001597 A3 20040608 (200441)

CZ 2003003480 A3 20040714 (200448)

KR 2004027512 A 20040401 (200451)

| KR | 2004027513 | Α  | 20040401 | (200451) |    |    |
|----|------------|----|----------|----------|----|----|
| AU | 2002319248 | A1 | 20021216 | (200452) |    |    |
| JΡ | 2004527586 | W  | 20040909 | (200459) |    | 84 |
| CN | 1520435    | Α  | 20040811 | (200476) |    |    |
| US | 2004241222 | A1 | 20041202 | (200480) |    |    |
| ZA | 2003008937 | Α  | 20050126 | (200513) |    | 57 |
| BR | 2002009699 | Α  | 20050201 | (200515) |    |    |
| IN | 2003001882 | P4 | 20041211 | (200530) | EN |    |
| MX | 2003011049 | A1 | 20040701 | (200545) |    |    |

## APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
| WO 2002098952 | A1   | WO 2002-EP6783 | 20020603 |
| EP 1392755    | A1   | EP 2002-748799 | 20020603 |
|               |      | WO 2002-EP6783 | 20020603 |
| NO 2003005264 | Α    | WO 2002-EP6783 | 20020603 |
|               |      | NO 2003-5264   | 20031127 |
| SK 2003001597 | A3   | WO 2002-EP6783 | 20020603 |
|               |      | SK 2003-1597   | 20020603 |
| CZ 2003003480 | A3   | WO 2002-EP6783 | 20020603 |
|               |      | CZ 2003-3480   | 20020603 |
| KR 2004027512 | Α    | KR 2003-715720 | 20031201 |
| KR 2004027513 | Α    | KR 2003-715722 | 20031201 |
| AU 2002319248 | A1   | AU 2002-319248 | 20020603 |
| JP 2004527586 | W    | WO 2002-EP6783 | 20020603 |
|               |      | JP 2003-502070 | 20020603 |
| CN 1520435    | Α    | CN 2002-812735 | 20020603 |
| US 2004241222 | A1   | WO 2002-EP6783 | 20020603 |
|               |      | US 2004-479031 | 20040617 |
| ZA 2003008937 | Α    | ZA 2003-8937   | 20031117 |
| BR 2002009699 | Α    | BR 2002-9699   | 20020603 |
|               |      | WO 2002-EP6783 | 20020603 |
| IN 2003001882 | P4   | WO 2002-EP6783 | 20020603 |
|               |      | IN 2003-CN1882 | 20031201 |
| MX 2003011049 | A1   | WO 2002-EP6783 | 20020603 |
|               |      | MX 2003-11049  | 20031201 |
|               |      |                |          |

# FILING DETAILS:

| PATENT NO  | KIND   | PATENT NO   |
|--|--|---|
| EP 1392755<br>SK 2003001597<br>CZ 2003003480<br>AU 2002319248<br>JP 2004527586 | A1 Based on A3 Based on A3 Based on A1 Based on W Based on | WO 2002098952<br>WO 2002098952<br>WO 2002098952<br>WO 2002098952<br>WO 2002098952 |
| BR 2002009699<br>MX 2003011049   | A Based on<br>Al Based on                                  | WO 2002098952<br>WO 2002098952  |

PRIORITY APPLN. INFO: EP 2001-202107 20010601

AN 2003-229291 [22] WPIDS

CR 2003-247851 [24]

AB WO 200298952 A UPAB: 20050715

NOVELTY - New colloidal carrier composition (I) comprises:

- (i) an active agent; and
- (ii) a lipid-polymer conjugate (Ia).

DETAILED DESCRIPTION - New colloidal carrier composition (I) comprises:

- (1) an active agent; and
- (2) a lipid-polymer conjugate (Ia) which is obtainable from

amphiphilic lipid that consists of at least one hydrophobic apolar moiety and hydrophilic polar head group, and polymer or its monomeric precursor, where the polymer is poly-(amino acid), poly-(amino acid derivative) or poly-(amino acid analog).

(Ia) provides long-circulating properties to (I).

ACTIVITY - Cytostatic; Antibacterial; Antiinflammatory.

USE - (I) is useful for providing a therapeutic agent, a biological agent, physiological agent, prophylactic or diagnostic agent (including imaging agents and radio-actively labeled compounds) in e.g. vesicular bilayer systems such as liposomes, niosomes and reversed vesicles, micellar systems, nanocapsules and nanospheres. (I) is also useful for passive targeting to sites of pathology (e.g. tumors, infection, inflammation) and for active targeting to cells in bloodstream, to endothelium. (I) is also useful as an artificial oxygen delivery system, blood-pool imaging and anti-fouling coating for biomaterials.

ADVANTAGE - The stability of liposomes prepared with (Ia) is improved as compared to that of conventional liposome preparations. (Ia) when incorporated into (I) provides long-circulating properties to these compositions. (Ia) is biodegradable and has reduced lipid-dose dependency as compared with polyethylene glycol-liposomes. An increased clearance after second injection of the composition is not always observed, and the reduction in blood circulation time is moderate. In an in vivo experimental arthritis model, one single intravenous injection of (I) appeared effective repeated injections of non-encapsulated corticosteroid compound or when encapsulated in conventional liposomes. Also, side effects associated with corticosteroid-based therapy will be reduced, due to reduction in the amount of corticosteroids that has to be administered.

DESCRIPTION OF DRAWING(S) - The figure shows a graphical representation of the mean values for the calculated percentage injected dose in blood samples versus time for polyethylene glycol-distearoyl phosphatidylethanolamine (PEG-DSPE)-containing liposomal preparations, having a different amount of lipid. Dwg.1/6

L15 ANSWER 11 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER:

2003-247851 [24]

CROSS REFERENCE:

2003-229291 [22]

DOC. NO. CPI:

C2003-063721

TITLE:

New lipid polymer conjugate useful for e.g. vesicular

bilayer systems for use e.g. in therapy,

WPIDS

comprises e.g. poly-amino acid derivative or poly-amino acid analogue polymer, and lipid attached to nitrogen or

carbon terminal of polymer.

DERWENT CLASS:

A23 A96 B07

INVENTOR(S):

BRUIN, P; DE BOER, L W T; DE VRINGER, T; HENNINK, W E; METSELAAR, J M; OUSSOREN, C; STORM, G; DE BRINGER, T;

METSELLAR, J M; DEBOER, L W T; HENNICK, W E; VRINGER, T D

PATENT ASSIGNEE(S):

(YAMA) YAMANOUCHI EURO BV; (BRUI-I) BRUIN P; (DBOE-I) DE BOER L W T; (HENN-I) HENNICK W E; (METS-I) METSELAAR J M; (OUSS-I) OUSSOREN C; (STOR-I) STORM G; (VRIN-I) VRINGER T

COUNTRY COUNT:

91

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2002098951 A2 20021212 (200324) \* EN 44

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AU BA BB BG BR BZ CA CN CO CR CU CZ DM DZ EC EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ OM PH PL RO SG SI SK TT UA US UZ VN YU ZA

#### APPLICATION DETAILS:

| PATENT NO KIND |    | APPLICATION    | DATE     |  |  |
|----------------|----|----------------|----------|--|--|
| WO 2002098951  | A2 | WO 2002-EP6432 | 20020603 |  |  |
| EP 1392756     | A2 | EP 2002-754661 | 20020603 |  |  |
|                |    | WO 2002-EP6432 | 20020603 |  |  |
| NO 2003005263  | Α  | WO 2002-EP6432 | 20020603 |  |  |
|                |    | NO 2003-5263   | 20031127 |  |  |
| SK 2003001598  | A3 | WO 2002-EP6432 | 20020603 |  |  |
|                |    | SK 2003-1598   | 20020603 |  |  |
| CZ 2003003479  | A3 | WO 2002-EP6432 | 20020603 |  |  |
|                |    | CZ 2003-3479   | 20020603 |  |  |
| AU 2002320851  | A1 | AU 2002-320851 | 20020603 |  |  |
| JP 2004527585  | M  | WO 2002-EP6432 | 20020603 |  |  |
|                |    | JP 2003-502069 | 20020603 |  |  |
| US 2004254352  | A1 | WO 2002-EP6432 | 20020603 |  |  |
|                |    | US 2004-479319 | 20040723 |  |  |
| BR 2002009695  | Α  | BR 2002-9695   | 20020603 |  |  |
|                |    | WO 2002-EP6432 | 20020603 |  |  |
| ZA 2003008938  | A  | ZA 2003-8938   | 20031117 |  |  |
| IN 2003001888  | P4 | WO 2002-EP6432 | 20020603 |  |  |
|                |    | IN 2003-CN1888 | 20031201 |  |  |
| MX 2003011050  | A1 | WO 2002-EP6432 | 20020603 |  |  |
|                |    | MX 2003-11050  | 20031201 |  |  |

## FILING DETAILS:

| PATENT NO     | KIND        | PATENT NO     |
|---------------|-------------|---------------|
| EP 1392756    | A2 Based on | WO 2002098951 |
| SK 2003001598 | A3 Based on | WO 2002098951 |
| CZ 2003003479 | A3 Based on | WO 2002098951 |
| AU 2002320851 | Al Based on | WO 2002098951 |
| JP 2004527585 | W Based on  | WO 2002098951 |
| BR 2002009695 | A Based on  | WO 2002098951 |
| MX 2003011050 | Al Based on | WO 2002098951 |

PRIORITY APPLN. INFO: EP 2001-202107 20010601

AN 2003-247851 [24] WPIDS

CR 2003-229291 [22]

AB WO 200298951 A UPAB: 20050715

NOVELTY - New lipid polymer conjugate (A) comprises at least one hydrophobic apolar moiety and a hydrophilic polar head group, and a polymer of specific formula or monomeric precursor having nitrogen (N) and carbon (C) terminal end groups.

The polymer is a poly-(amino acid), poly-(amino acid derivative) or a poly-(amino acid) analog.

The lipid is attached to N or C terminal of the polymer. DETAILED DESCRIPTION - A lipid polymer conjugate comprises at least one hydrophobic apolar moiety and a hydrophilic polar head group, and a polymer of formula -(NHCHR(CH2)mCO)n- (I) or monomeric precursor having nitrogen (N) and carbon (C) terminal end groups.

The polymer is a poly-(amino acid), poly-(amino acid derivative) or a poly-(amino acid) analog.

The lipid is attached to N or C terminal of the polymer.

The lipid polymer is obtainable from an amphiphilic lipid.

R = H, -CH3, -CHCH3OR, -(CH2)xOR1, -(CH2)x-CO-NHR1, -(CH2)x-NH-CO-R1, -(CH2)x-SOyCH3, OR-(CH2)xCOOH;

R1 = hydrogen or 1-4C alkyl optionally substituted with one or more hydroxy groups or one di 1-4C alkylamine group;

x = 0-4;

m = 1 or 0; and

y = 1 or 2.

USE - (A) are used for inclusion into a colloidal carrier composition e.g. vesicular bilayer systems, such as liposomes, niosomes and reversed vesicles, micellar systems, nanocapsules and nanospheres and for use in therapy, diagnosis and prophylaxis.

ADVANTAGE - The polymer lipid conjugates (A) exhibits ability to reduce zeta potential, thus demonstrates the polymer grafting shielded the surface charge. The polymer lipid conjugates are biodegradable and hence provide no risk of accumulation in cells of animal or human body. (A) exhibits reduced lipid dose dependency. An increased clearance after second injection of the lipid polymer conjugate composition is not observed and the reduction in blood circulation time is moderate.

DESCRIPTION OF DRAWING(S) - The figure shows a graph showing the mean values for the calculated percentage injected dose in blood samples versus time for polyethylene glycol-poly(2-hydroxyethyl)-L-asparagine containing liposomal preparation having different amount of total lipid. Dwg.1/6

L15 ANSWER 13 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER:

2002-434879 [46] WPIDS

DOC. NO. NON-CPI:

N2002-342354

DOC. NO. CPI:

C2002-123416

TITLE:

Biocompatible material useful for e.g. controlling

cellular growth comprises at least two component surface.

DERWENT CLASS:

A18 A23 A25 A96 B04 B07 D16 D22 P34

INVENTOR(S):

ALTANKOV, G; JANKOVA, K; JONSSON, G; THOM, V; ULBRICHT, M

PATENT ASSIGNEE(S):

(SURF-N) SURFARC APS; (BIOS-N) BIOSURF APS; (ALTA-I) ALTANKOV G; (JANK-I) JANKOVA K; (JONS-I) JONSSON G;

(THOM-I) THOM V; (ULBR-I) ULBRICHT M

COUNTRY COUNT:

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2002015955 A2 20020228 (200246) \* EN 217

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001081758 A 20020304 (200247)

98

A2 20030716 (200347) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

US 2005053642 A1 20050310 (200519)

#### APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
|               |      |                |          |
| WO 2002015955 | A2   | WO 2001-DK557  | 20010823 |
| AU 2001081758 | A    | AU 2001-81758  | 20010823 |
| EP 1326655    | A2   | EP 2001-960202 | 20010823 |
|               |      | WO 2001-DK557  | 20010823 |
| US 2005053642 | A1   | WO 2001-DK557  | 20010823 |
|               |      | US 2003-362677 | 20030815 |

## FILING DETAILS:

| PATENT NO | KIND | PATENT NO                      |
|-----------|------|--------------------------------|
|           |      | WO 2002015955<br>WO 2002015955 |

PRIORITY APPLN. INFO: DK 2000-1250

20000823

AN 2002-434879 [46] WPIDS

AB WO 200215955 A UPAB: 20040408

NOVELTY - Biocompatible material comprises a surface comprising at least two components such as a hydrophobic substratum and a macromolecule of hydrophobic nature.

DETAILED DESCRIPTION - Biocompatible material comprises a substratum (A) contacted by at least one macro-molecule. The material has a first advancing contact angle (a). (A) has a second advancing contacting angle b0 when not contacted by a macromolecule and another second advancing contact angle bsat, when the substratum is saturated by the macromolecules. The advancing contact angles are measured using water and air saturated by water vapor. The bsat does not change when the substratum is contacted by further macromolecules by a chemical bond. The relation between the advancing contact angles is R = (b0 - a)/(b0 - bsat) where R is 0 - less than 0.4.

INDEPENDENT CLAIMS are included for the following:

- (1) use of the material in the manufacture of an implantable organ or its part; and
  - (2) producing the material by:
- (i) contacting the substratum having a second contact angle with a composition comprising several macromolecules; and
- (ii) providing a biocompatible material comprising a substratum contacted by several macromolecules.

ACTIVITY - Antiinfertility.

MECHANISM OF ACTION - None given.

USE - For controlling cellular growth, cellular proliferation, and/or cellular differentiation; separating and/or isolating biological material; producing a biohybrid organ; diagnosis or carrying out therapy, carrying out surgery of human or animal or their parts; as a carrier for in vivo delivery of a medicament to a human or animal body (claimed); as cell culture dishes, bioreactors, implants, biohybrid organs e.g. pacemaker etc.; to create bio-compatible surfaces suitable for use in emerging technologies e.g. the construction and application of the surface architectures of biomaterials with innovative functionalities such as bioartificial pancreas, liver or kidney; to improve the implantation rates after in vitro fertilization; to treat and/or prevent infertility or early pregnancy loss; to provide a container capable of mimicking an endomaterial environment of a female uterus; to enhance fertility potential of animal oocytes e.g. sports, zoo, pet and farm animals; in a dialysis membrane; for making tissue engineered constructs, valves and vessels; to provide polymer-based drug release systems e.g. systems based on implantable materials; for bone reconstruction with

tissue engineering vascularized bone; for engineering composite bone and cartilage; to increase the mechanical strength and liability of e.g. heart valve leaflets and other engineered tissues; for growing vertebrate cells e.g. human cells including human skin cells; in skin grafting.

ADVANTAGE - (A) in cooperation with the macromolecule maintains, improves and/or stabilizes the biologically active form or its conformation. The biologically active compound improves contact between the material and a biological entity e.g. biological cell or virus or their parts, including a polypeptide or its part, nucleic acid, carbohydrate and/or lipid. The material does not induce an acute or chronic inflammatory response and does not prevent a proper differentiation of implant surrounding tissue. The method is simple and inexpensive. The surfaces can be used as cell culture dishes, bioreactors, implants etc. without the need of extensive development of new polymers and biocompatibility screening, ensures spatial separation of e.g. xenogenic and/or allogenic cells from the host immune system. The method increases the rate of maturation of immature oocytes and potential of fertilization of oocytes, minimizes incubation-time, and improves the quality of incubated oocytes. The degree of modification resulting from macromolecule including PEG attachment does not reduces the permeability of the membranes, thus suitable for the application as haemodialysis membrane. The tissue engineered constructs have improved mechanical strength and flexibility while retains biocompatible properties of the material. The valves and vessels withstand repeated stress and stirring. Dwg.0/31

L15 ANSWER 14 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2001-514501 [56]

DOC. NO. CPI: C2001-153732

TITLE:

Composition comprising a combination of an oxidizing and/or reducing agent, a protein-denaturing agent, and a

hapten, useful for treating neoplasms, tumors, and

WPIDS

cancers.

DERWENT CLASS: '

B05 D16

INVENTOR(S):

YU, B

94

PATENT ASSIGNEE(S):

(YUBB-I) YU B

COUNTRY COUNT:

PATENT INFORMATION:

| PAT | CENT | ИО   |      |       | KIN           | 1D I | DATE          | 2   | V   | VEE  | K                |    | LΑ | I   | ?G |    |    |    |    |    |    |    |    |
|-----|------|------|------|-------|---------------|------|---------------|-----|-----|------|------------------|----|----|-----|----|----|----|----|----|----|----|----|----|
| WO  | 200  | 1052 | 2868 | <br>3 | A1            | 200  | 0107          | 726 | (20 | 001  | 56) <sup>1</sup> | El |    | 83  | -  |    |    |    |    |    |    |    |    |
|     | RW:  | ΑT   | BE   | CH    | CY            | DE   | DK            | EΑ  | ES  | FI   | FR               | GB | GH | GM  | GR | ΙE | IT | ΚE | LS | LU | MC | MW | MZ |
|     |      | NL   | OA   | PT    | SD            | SE   | $\mathtt{SL}$ | SZ  | TR  | TZ   | UG               | ZW |    |     |    |    |    |    |    |    |    |    |    |
|     | W:   | ΑE   | AG   | AL    | AM            | ΑT   | ΑU            | ΑZ  | BA  | ВВ   | BG               | BR | BY | BZ  | CA | CH | CN | CR | CU | CZ | DE | DK | DM |
|     |      | DZ   | EE   | ES    | FI            | GB   | GD            | GE  | GH  | GM   | HR               | HU | ID | IL  | IN | IS | JΡ | ΚE | KG | ΚP | KR | ΚZ | LC |
|     |      | LΚ   | LR   | LS    | LT            | LU   | LV            | MA  | MD  | MG   | MK               | MN | MW | ΜX  | ΜZ | NO | NZ | PL | PT | RO | RU | SD | SE |
|     |      | SG   | SI   | SK    | $\mathtt{SL}$ | TJ   | TM            | TR  | TT  | TZ   | UA               | UG | UZ | VN  | YU | ZA | ZW |    |    |    |    |    |    |
| ΑU  | 200  | 1030 | 097  | 7     | Α             | 200  | 0107          | 731 | (20 | 001  | 71)              |    |    |     |    |    |    |    |    |    |    |    |    |
| US  | 2002 | 2044 | 1919 | 9     | A1            | 200  | 0204          | 118 | (20 | 0022 | 28)              |    |    |     |    |    |    |    |    |    |    |    |    |
| CN  | 143  | 1909 | 9    |       | Α             | 200  | 030           | 723 | (20 | 003  | 65)              |    |    |     |    |    |    |    |    |    |    |    |    |
| JP  | 2004 | 4505 | 5009 | 9     | W             | 200  | 0402          | 219 | (20 | 004  | 14)              |    | 2  | 223 |    |    |    |    |    |    |    |    |    |
| US  | 681  | 1788 | 3    |       | В2            | 200  | 0413          | L02 | (20 | 004  | 72)              |    |    |     |    |    |    |    |    |    |    |    |    |
| US  | 200  | 5118 | 3187 | 7     | A1            | 200  | 0506          | 502 | (20 | 005  | 37)              |    |    |     |    |    |    |    |    |    |    |    |    |

## APPLICATION DETAILS:

| PATENT NO     | KIND | APPLICATION    | DATE     |
|---------------|------|----------------|----------|
| WO 2001052868 | A1   | WO 2001-US1737 | 20010118 |
| AU 2001030977 | A    | AU 2001-30977  | 20010118 |

| US | 2002044919 | A1 | Provisional | US | 2000-177024P | 20000119 |
|----|------------|----|-------------|----|--------------|----------|
|    |            |    |             | US | 2001-765060  | 20010117 |
| CN | 1431909    | Α  |             | CN | 2001-806830  | 20010118 |
| JP | 2004505009 | W  |             | JP | 2001-552915  | 20010118 |
|    |            |    |             | WO | 2001-US1737  | 20010118 |
| US | 6811788    | B2 | Provisional | US | 2000-177024P | 20000119 |
|    |            |    |             | US | 2001-765060  | 20010117 |
| US | 2005118187 | A1 | Provisional | US | 2000-177024P | 20000119 |
|    |            |    | CIP of      | US | 2001-765060  | 20010117 |
|    |            |    |             | US | 2004-973798  | 20041025 |

#### FILING DETAILS:

| PATENT NO            | KIND                             | PATENT NO                    |  |  |
|----------------------|----------------------------------|------------------------------|--|--|
| AU 2001030977        | A Based on                       | WO 2001052868                |  |  |
| JP 2004505009        | W Based on                       | WO 2001052868                |  |  |
| US 2005118187        | Al CIP of                        | US 6811788                   |  |  |
| PRIORITY APPLN. INFO | : US 2000-177024P<br>2001-765060 | 20000119; US<br>20010117; US |  |  |

2004-973798 AN 2001-514501 [56] WPIDS

AB WO 200152868 A UPAB: 20011001

NOVELTY - A composition (I) comprising a combination of an oxidizing or reducing agent, a protein-denaturing agent, and a hapten, is new.

20041025

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a kit comprising the combination (I);
- (2) an article of manufacture comprising:
- (a) packaging material;
- (b) the combination above; and
- (c) a label indicating that the article is for treating neoplasms;
- (3) a method for treating neoplasm in a mammal comprising in situ administration to the neoplasm of a mammal, a hapten and a coagulation agent or treatment that causes coagulation of the neoplasm (an autologous immune response is generated against the neoplasm).

ACTIVITY - Cytostatic.

31 advanced stage IV liver cancer patients were treated using the new combination. Prior to procedure, patients were given a mild sedative or painkiller. Patients were calmed thoroughly and were also monitored by modern medial imaging. With local anesthesia, percutaneous puncture was administered directly into the tumor using a spinal needle connected to a high-power syringe containing a combination of ethanol, H2O2, anticancer drug AraC (8 mg/ml) and hemotoxilin (5 mg/ml). Combination was injected directly into the tumor and distributed throughout the matrix of the whole tumor. Sonic imaging showed the stranger echo imaging which indicated the coagulation area.

Following coagulation lysis and tumor cell death monitored by sonic imaging, which showed liquefied echo, tumor started to shrink and disappear. Normal tissues grew replacing the tumor. The process was monitored by medical imaging systems. The amount of the ingredients of the combination injected into the tumor was determined by the diameter of tumors (cm) with 2 ml of the combination for each centimeter.

Procedure was repeated in 1-2 weeks. On average, each patient was treated with the injection for 3 times. No severe side effects for all the treated patients was observed, although some patients experienced tolerable pain the injection site while a few had light fever during the first week. All side effects disappeared in about 1 week. No serious complications happened in any cases.

MECHANISM OF ACTION - Gene therapy.

USE - The combination and the methods are useful for treating neoplasms, tumors, and cancers, including neoplasm or cancer of the e.g. adrenal gland, anus, auditory nerve, bile ducts, bladder, bone, brain, breast, bruccal, central nervous system, cervix, colon, ear, endometrium, esophagus, eye, eyelids, fallopian tube, gastrointestinal tract, head and neck, heart, kidney, larynx, liver, lung, or mandible.

The combination and methods may further be used in treating tumors of mesenchymal origin (e.g. connective tissue and derivatives, or endothelial and related tissues blood vessels), epithelial origin (stratified squamous carcinoma, or basal cells of skin or adenexa), and tumors derived from more than one neoplastic cell types derived from more than one germ layers.

L15 ANSWER 15 OF 38 MEDLINE on STN
ACCESSION NUMBER: 2001673979 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11718771
TITLE: PubMed ID: 11718771
Orienting otolith-ocular reflexes in the rabbit during

static and dynamic tilts and off-vertical axis rotation.

AUTHOR: Maruta J; Simpson J I; Raphan T; Cohen B

CORPORATE SOURCE: Departments of Neurology and Physiology and Biophysics,

Mount Sinai School of Medicine, 1 East 100th Street, Box

1135, New York, NY 10029, USA.

SOURCE: Vision research, (2001) 41 (25-26) 3255-70.

Journal code: 0417402. ISSN: 0042-6989.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Space Life Sciences

ENTRY MONTH: 200203

ENTRY DATE: Entered STN: 20011126

Last Updated on STN: 20020413 Entered Medline: 20020311

AB Orienting otolith-ocular reflexes were assessed in rabbits using static tilt, off-vertical axis rotation (OVAR) and sinusoidal oscillation about earth-horizontal axes. In all paradigms, head pitch produced ocular counter-pitch and vergence, and head roll produced ocular counter-roll and conjugate yaw version. Thus, vergence and version are essential components of orienting reflexes along the naso-occipital and bitemporal axes. Vergence and version caused misalignment between the axes of eye and head movement during pitch and roll head movements. Semicircular canal input broadened the band-pass of these orienting reflexes, which would make them more appropriate when compensating for head movement during active motion.

L15 ANSWER 17 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2000-071650 [06] WPIDS

CROSS REFERENCE: 1996-393530 [39]; 1997-393702 [36]; 1998-145264 [13];

1998-457256 [39]; 1998-495982 [42]; 1999-204741 [17]; 2000-147218 [13]; 2001-225814 [23]; 2002-089133 [12];

2002-105080 [14]

DOC. NO. CPI: C2000-020448

TITLE: Polymeric assay film for direct colorimetric detection of

small molecules such as pathogens.

DERWENT CLASS: A89 B04 D16 J04

INVENTOR(S): CHARYCH, D; NAGY, J; SPEVAK, W

PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA

COUNTRY COUNT: 1

PATENT INFORMATION:

| PATENT NO  | KI | ND DATE  | WEEK       | LA | PG |
|------------|----|----------|------------|----|----|
|            |    |          |            |    |    |
| US 6001556 | Α  | 19991214 | (200006) * | 20 | a  |

## APPLICATION DETAILS:

| PATENT NO  | KIND                          | APPLICATION  | DATE   |
|------------|-------------------------------|--|--|
| us 6001556 | A CIP of<br>CIP of<br>Cont of | US 1992-976697<br>US 1992-982189<br>US 1993-159927<br>US 1996-592724 | 19921113<br>19921125<br>19931130<br>19960126 |

PRIORITY APPLN. INFO: US 1993-159927 19931130; US 1992-976697 19921113; US 1992-982189 19921125; US 1996-592724 19960126

AN 2000-071650 [06] WPIDS

CR 1996-393530 [39]; 1997-393702 [36]; 1998-145264 [13]; 1998-457256 [39]; 1998-495982 [42]; 1999-204741 [17]; 2000-147218 [13]; 2001-225814 [23]; 2002-089133 [12]; 2002-105080 [14]

AB US 6001556 A UPAB: 20040928

NOVELTY - Polymeric assay films for direct colorimetric detection tests of small molecules, are new.

DETAILED DESCRIPTION - A polymerized **bilayer** film (I) comprises:

- (1) a conjugated polymer backbone (comprising a number of polymerized diacetylene monomers);
- (2) linker groups (which are covalently conjugated to the polymer backbone);
- (3) ligands (either sialic acid and/or carbohydrates with ordering heads groups covalently conjugated to the linker groups) with direct affinity for an analyte; and
  - (4) a support structure.

The ordering head groups are bound to the surface of the conjugated polymer backbone in positions not occupied by the linker groups. The polymerized bilayer film undergoes a detectable color change upon binding of the analyte to the ligands.

INDEPENDENT CLAIMS are also included for the following:

- (1) a method (II) of producing (I), comprising:
- (a) providing:
  - (i) ligands (carbohydrates) with a direct affinity for an analyte;
  - (ii) linker groups with 2 terminal ends;
  - (iii) lipid monomers;
  - (iv) lipid monomers comprising ordering head groups; and
  - (v) a support surface;
- (b) attaching the ligands to the lipid monomers so that the ligands are attached to one end of the linkers and the lipid monomers are attached to the other (to produce monomer-linear structural unit-ligand groups);
- (c) mixing the monomer-linear structural unit-ligand groups with lipid monomers comprising ordering heads;
- (d) spreading the mixture from step (c) on the support to form a bilayer film; and
- (e) polymerizing the bilayer film (to form the polymerized bilayer film (I)); and
- (2) a method for detecting an analyte, comprising contacting (I) with a sample thought to contain the analyte and detecting a color change in (I) (a color change is indicative of the presence of the analyte).
- USE (I) may be used for the direct detection of small molecules such as pathogens (e.g. influenza viruses, herpes virus, human

immunodeficiency virus (HIV), coronavirus, encephalomyelitis, chlamydia, rotavirus, polyomavirus, Streptococcus, Salmonella, sendai virus, mumps virus, Newcastle Disease virus, myxovirus, Escherichia coli, encephalomyocarditis virus and Plasmodium (claimed)). Other substances such as industrial materials, enzymes, hormones, cell wall fragments, blood components, disease indicators, cell components, antibodies, lectins and genetic material may also be detected using (I).

(I) also has application in feedstock and effluent monitoring, drug development and other types of medical testing.

ADVANTAGE - The use of (I) is easily automated, especially if a spectrometer is used to detect color changes. A multiple well system may be produced from (I) which allows inexpensive screening and sequential testing for analytes. (I) represents a new approach to the direct detection of a material using color changes in a monomolecular film which occurs when specifically bound to the target molecule. (I) is simple and inexpensive to produce.

(I) provides the advantages of both an immunoassay and chemical analysis in a single system. It has the inherent direct assay advantages of analytical chemistry methods and has a substantial environmental range of testing beyond that of immunoassays. This allows accommodation of various analytes in their most advantageous environmental parameters. Additionally, (I) allows rigorous direct analysis to occur even in very narrow environmental ranges, previously unavailable with analytical chemical techniques. The speed and simplicity of the color change indicator of (I) are its hallmark advantages. Dwg.0/6

L15 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

1999:243267 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

131:15441

TITLE:

Effect of PEG-lipid conjugates on the phase behavior

of phosphatidylethanolamine dispersions

AUTHOR(S):

Koynova, R.; Tenchov, B.; Rapp, G.

CORPORATE SOURCE:

Institute of Biophysics, Bulgarian Academy of

Sciences, Sofia, 1113, Bulg.

SOURCE:

Colloids and Surfaces, A: Physicochemical and Engineering Aspects (1999), 149(1-3), 571-575

CODEN: CPEAEH; ISSN: 0927-7757

PUBLISHER:

Elsevier Science B.V.

DOCUMENT TYPE:

Journal English

LANGUAGE:

The phase behavior of binary mixts. of hydrated dielaidoylphosphatidylethanolamine (DEPE) with two different PEG-lipid conjugates at a molar fraction below 0.2 has been studied by using time-resolved X-ray diffraction, and partial phase diagrams have been constructed. The studied conjugates comprise two saturated hydrocarbon acyl chains 14 carbon atoms long and PEG550 or PEG5000 chains covalently attached to a phosphoethanolamine polar head group, DMPE(PEG550) and DMPE(PEG5000), resp. When added in small amts. (10-20 mol%) to DEPE aqueous dispersions, both PEG-lipids favor the lamellar liquid crystalline (L $\alpha$ ) phase at the expense of the lamellar gel (L $\beta$ ) and the inverted hexagonal (HII) phases. One of the conjugates, DMPE(PEG550), shifts the  $L\alpha$ -HII transition of DEPE to higher temps. by 2.5°C per mol% PEG-lipid, and induces the spontaneous formation of a cubic phase of space group Im3m in the DEPE dispersions. The cubic phase intrudes between the lamellar liquid crystalline and the inverted hexagonal

phases in the DEPE/DMPE(PEG550) phase diagram. Low amts. of the DMPE(PEG5000) conjugate only shift the L $\alpha$ -HII transition of DEPE to higher temps., at 5.2°C per mol% PEG-lipid, but does not promote the formation of addnl. phases. The resp. slopes for the  $L\beta-L\alpha$ , transition temperature depression are 10-15 times smaller. At

> 15 mol% DMPE(PEG550) and at > 5 mol% DMPE(PEG5000), the non-lamellar phases are eliminated from the phase diagrams. Structural data on the organization of the pure hydrated PEG-lipid conjugates are also provided, suggesting that these lipids form micelles and lamellae.

REFERENCE COUNT:

16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:471436 CAPLUS

DOCUMENT NUMBER: 129:78811

TITLE: Receptor membranes.

Cornell, Bruce Andrew; Braach-maksvytis, Vijolrta INVENTOR(S):

Lucija Brinislava

PATENT ASSIGNEE(S): Australian Membrane and Biotechnology Research

Institute, Australia

SOURCE: U.S., 14 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. |   | DATE     |
|------------------------|------|----------|-----------------|---|----------|
|                        |      |          |                 |   |          |
| US 5766960             | Α    | 19980616 | US 1995-449895  |   | 19950523 |
| US 5436170             | Α    | 19950725 | US 1990-473932  |   | 19900125 |
| US 5693477             | Α    | 19971202 | US 1995-447569  |   | 19950523 |
| US 5741712             | Α    | 19980421 | US 1995-448178  |   | 19950523 |
| PRIORITY APPLN. INFO.: |      |          | AU 1987-3346    | Α | 19870727 |
|                        |      |          | AU 1987-3348    | Α | 19870727 |
|                        |      |          | AU 1987-3453    | Α | 19870731 |
|                        |      |          | AU 1987-4478    | Α | 19870921 |
|                        |      |          | US 1990-473932  | Α | 19900125 |
|                        |      |          | WO 1988-AU273   | W | 19880727 |

AB A membrane comprising a closely packed array of self-assembling amphiphilic mols., and is characterized in that it incorporates a plurality of ion channels, and/or at least a proportion of the self-assembling mols. comprise a receptor mol. conjugated with a supporting entity. The ion channel is selected from the group consisting of peptides capable of forming helixes and aggregates thereof, coronands, cryptands, podands and combinations thereof. In the amphiphilic mols. comprising a receptor mol. conjugated with a supporting entity, the receptor mol. has a receptor site and is selected from the group consisting of Igs, antibodies, antibody fragments, dyes, enzymes and lectins. "The supporting entity is selected from the group consisting of a lipid head group, a hydrocarbon chain(s), a cross-linkable mol. and a membrane protein. The supporting entity is attached to the receptor mol. at tan end remote from the receptor site. In preferred embodiments the ion channel is gramicidin A, and is preferable gated. Such membranes may be used in the formation of sensing devices.

REFERENCE COUNT: THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 25 OF 38 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 93229518 MEDLINE DOCUMENT NUMBER: PubMed ID: 8471621

TITLE: Lipid-amphotericin B complex structure in solution: a

possible first step in the aggregation process in cell

AUTHOR: Balakrishnan A R; Easwaran K R

CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science,

Bangalore.

SOURCE:

Biochemistry, (1993 Apr 20) 32 (15) 4139-44.

Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199305

ENTRY DATE:

Entered STN: 19930604

Last Updated on STN: 19930604 Entered Medline: 19930517

AΒ The interactions between the polyene antibiotic amphotericin B with dipalmitoylphosphatidylcholine were investigated in vesicles (using circular dichroism) and in chloroform solution (using circular dichroism and 1H, 13C, and 31P nuclear magnetic resonance). The results show that amphotericin B readily aggregates in vesicles and that the extent of aggregation depends on the lipid:drug concentration ratio. Introduction of sterol molecules into the membrane hastens the process of aggregation of amphotericin B. In chloroform solutions amphotericin B strongly interacts with phospholipid molecules to form a stoichiometric complex. The results suggest that there are interactions between the conjugated heptene stretch of amphotericin B and the methylene groups of lipid acyl chains, while the sugar moiety interacts with the phosphate head group by the formation of a hydrogen bond. A model is proposed for the lipid-amphotericin B complex, in which amphotericin B interacts equally well with the two lipid acyl chains, forming a 1:1 complex.

L15 ANSWER 27 OF 38 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 93123198
DOCUMENT NUMBER: PubMed ID

93123198 MEDLINE PubMed ID: 1478927

TITLE:

Induction of vesicle-to-micelle transition by bile salts

for DOPE vesicles incorporating immunoglobulin G.

AUTHOR:

Lee E O; Kim J G; Kim J D

CORPORATE SOURCE:

Department of Chemical Engineering and Bioprocess ERC,

Korea Advanced Institute of Science and Technology, Taejon.

SOURCE:

Journal of biochemistry, (1992 Nov) 112 (5) 671-6. Journal code: 0376600. ISSN: 0021-924X.

PUB. COUNTRY:

Japan

DOCUMENT TYPE: Jou

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199302

ENTRY DATE:

Entered STN: 19930226

Last Updated on STN: 19930226 Entered Medline: 19930208

AΒ The vesicle-to-micelle transition of immunoliposomes formed by dioleoylphosphatidyl-ethanolamine (DOPE) and palmitoyl-immunoglobulin G (p-IgG) was investigated in the presence of bile salts and conjugated bile salts. Turbidity and the release of calcein from liposomes were measured as a function of the amount of bile salts added and compared with the solubilizing profiles of the salts according to the number and configurational state of hydroxy groups in the cholate. The solubilizing phenomena by bile salts conjugated with glycine or taurine were investigated in comparison with non-conjugated bile salts. The solubilizing effect of bile salts on the bilayer of immunoliposomes increased remarkably with the number of hydroxy groups, but was not influenced by the configurational state of the hydroxy group. The half-maximal concentration of bile salts, defined as the concentration giving the half-maximum turbidity of liposome solutions, decreased with hydrophobicity in the phosphatidylcholine (PC) bilayer. increase in the hydrophobicity of bile salts induces the ability to permeabilize and solubilize phospholipid vesicles. In the case of PC or

PE liposome bilayers with inserted protein, bile salts conjugated with taurine or glycine had lower hydrophobicity than non-conjugated bile salts and showed a lower half-maximal concentration. The conjugated bile salts are believed to interact with lipids and solubilize the bilayers, while the head groups of bile salts interact with the inserted protein and extract it from the lipid bilayer.

L15 ANSWER 28 OF 38 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 1989-061259 [08] WPIDS

DOC. NO. NON-CPI: N1989-046623 DOC. NO. CPI: C1989-027144

TITLE: Receptor membrane for bio-sensors - comprising

a closely packed array of self-assembling amphiphilic molecules having ion channels and/or receptor molecules.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): BRAACH-MAKSVYTIS, V L B; CORNELL, B A; BRAACH-MAKSVYTIS,

V L; BRAACHMAKS, V L B; BRAACH-MAKSVYTIS, V

PATENT ASSIGNEE(S): (CSIR) COMMONWEALTH SCI & IND RES ORG; (AUME-N) AUSTRALIA

MEMBRANE & BIOTECHNOLOGY RES INST; (AUME-N) AUSTRALIAN

MEMBRANE & BIOTECHNOLOGY INST

COUNTRY COUNT:

PATENT INFORMATION:

| PAT | TENT NO                  | KII | ND DATE  | WEEK         | LA | PG |
|-----|--------------------------|-----|----------|--------------|----|----|
| WO  | 8901159                  | Α   | 19890209 | (198908) * 1 | EN | 40 |
|     | RW: AT BE CH W: AU JP US | DE  | FR GB IT | LI LU NL SI  | Ē  |    |
| AU  | 8821279                  | Α   | 19890301 | (198923)     |    |    |
| ΕP  | 382736                   | Α   | 19900822 | (199034)     |    |    |
|     | R: AT BE CH              | DE  | FR GB IT | LI LU NL SI  | Ξ  |    |
| JP  | 03503209                 | W   | 19910718 | (199135)     |    |    |
| ΕP  | 382736                   | В1  | 19941102 | (199442)     | ΞN | 24 |
|     | R: AT BE CH              |     |          |              | Ξ  |    |
|     | 3852036                  |     |          |              |    |    |
|     | 382736                   |     |          |              |    |    |
|     | 1335879                  |     |          |              |    |    |
|     | 5436170                  |     |          |              |    |    |
| JP  | 2682859                  | B2  | 19971126 | (199801)     |    | 14 |
|     | 5693477                  |     |          |              |    |    |
|     | 5741712                  |     |          |              |    | 13 |
| US  | 5766960                  | Α   | 19980616 | (199831)     |    |    |
|     |                          |     |          |              |    |    |

# APPLICATION DETAILS:

| PATENT NO |    | KINI      | )         | AI      | APPLICATION |              |          |  |  |
|-----------|----|-----------|-----------|---------|-------------|--------------|----------|--|--|
|           | WO | 8901159   | A         |         | WO          | 1988-AU273   | 19880727 |  |  |
|           | EΡ | 382736    | Α         |         | EP          | 1988-907164  | 19880727 |  |  |
|           | JP | 03503209  | W         |         | JP          | 1988-506329  | 19880727 |  |  |
|           | ΕP | 382736    | B1        |         | EP          | 1988-907164  | 19880727 |  |  |
|           |    |           |           |         | WO          | 1988-AU273   | 19880727 |  |  |
|           | DE | 3852036   | G         |         | DE          | 1988-3852036 | 19880727 |  |  |
|           |    |           |           |         | EP          | 1988-907164  | 19880727 |  |  |
|           |    |           |           |         | WO          | 1988-AU273   | 19880727 |  |  |
|           | ΕP | 382736    | <b>A4</b> |         | EP          | 1988-907164  |          |  |  |
|           | CA | 1335879 , | С         |         | CA          | 1988-573217  | 19880727 |  |  |
|           | US | 5436170   | Α         |         | WO          | 1988-AU273   | 19880727 |  |  |
|           |    |           |           |         | US          | 1990-473932  | 19900125 |  |  |
|           | JP | 2682859   | B2        |         | JP          | 1988-506329  | 19880727 |  |  |
|           |    |           |           |         | WO          | 1988-AU273   | 19880727 |  |  |
|           | US | 5693477   | Α         | Cont of | US          | 1990-473932  | 19900125 |  |  |
|           |    |           |           |         |             |              |          |  |  |

|    |         |   |     | Ţ    | US | 1995-447569 | 19950523 |
|----|---------|---|-----|------|----|-------------|----------|
| US | 5741712 | Α | Div | ex 1 | US | 1990-473932 | 19900125 |
|    |         |   |     | τ    | US | 1995-448178 | 19950523 |
| US | 5766960 | Α | CIP | of ( | US | 1990-473932 | 19900125 |
|    |         |   |     | ī    | US | 1995-449895 | 19950523 |

## FILING DETAILS:

AΒ

| PATENT NO       | KIND               | PATENT NO    |
|-----------------|--------------------|--------------|
| EP 382736       | B1 Based on        | WO 8901159   |
| DE 3852036      | G Based on         | EP 382736    |
|                 | Based on           | WO 8901159   |
| US 5436170      | A Based on         | WO 8901159   |
| JP 2682859      | B2 Previous Publ.  | JP 03503209  |
|                 | Based on           | WO 8901159   |
| US 5693477      | A Cont of          | US 5436170   |
| US 5741712      | A Div ex           | US 5436170   |
| US 5766960      | A CIP of           | US 5436170   |
| PRIORITY APPLN. | INFO: AU 1987-4478 | 19870921; AU |
|                 | 1987-3346          | 19870727; AU |
|                 | 1987-3348          | 19870727; AU |
|                 | 1988-21279         | 19870728; AU |
|                 | 1987-3453          | 19870731     |
| AN 1989-061259  | [08] WPIDS         |              |

8901159 A UPAB: 19960520

A membrane comprising a closely packed array of self-assembling amphiphilic molecules is claimed characterised in that (1) the membrane includes ion channels selected from peptides capable of forming helices and aggregates, podands, coronands, cryptands and combinations and/or (2) at least a proportion of the self-assembling amphiphilic molecules comprise a receptor molecule conjugated with a supporting entity, the receptor molecule having a receptor site and being selected from immunoglobulins, antibodies, antibody fragments, dyes, enzymes and lectins, the supporting entity being selected from a lipid head gp., a hydrocarbon chain, a cross-linkable molecule and a membrane protein, the supporting entity being conjugated with the receptor molecule at an end remote from the receptor site.

Pref. the ion channels are gramicidin or analogues. Also claimed is a biosensor comprising a membrane bilayer attached to a solid surface, the bilayer having an upper and lower layer, the lower layer being adjacent the solid surface and being provided with gps. reactive with the solid surface or with gps. provided on this, each layer of the bilayer being composed of self-assembling amphiphilic molecules and gramicidin monomers, and where a receptor moiety is attached to the gramicidin monomers in the upper layer. The solid surface is pref. a palladium-coated glass electrode.

USE/ADVANTAGE - The membranes are used partic. for the production of biosensors. They have a high density of receptor sites and serve as highly selective binding surfaces to which molecular species to be detected will bind.

0/6

Dwg.0/6

ABEQ EP 382736 B UPAB: 19941212

A membrane bound to a solid non-porous surface, the membrane comprising a closely packed array of self-assembling amphiphillic molecules and characterised in that:

- (1) the membrane includes a plurality of ion channels which are peptides capable of forming helices and aggregates thereof, a podand, coronand, cryptand or a combination thereof; and
  - (2) at least a proportion of the self-assembling amphiphillic

molecules comprise a receptor molecule conjugated with a supporting entity, the receptor molecule having a receptor site and being an immunoglobulin, antibody, antibody fragment, dye, enzyme or lectin;

the supporting entity being a lipid head group, a hydrocarbon chain(s), a cross-linkable molecule or a membrane protein and being conjugated with the receptor molecule at an end remote from the receptor site.

Dwg.0/6

ABEQ US 5436170 A UPAB: 19950905

Membrane comprises a closely packed array of self-assembling amphiphilic molecules, e.g. peptides that form helices and/or aggregates, such that numerous ion channels are present in the structure and at least part of the structure comprises a receptor (e.g. immunoglobulin, antibody or its active binding fragment, enzyme or lectin) conjugated with a hydrocarbon chain or membrane protein at a location remote from the receptor's active site.

USE - The prods. are components of selective biosensors. ADVANTAGE - The membrane is mounted on a solid supporting surface to provide robustness and avoid fragility. Dwg.0/6

ABEQ US 5693477 A UPAB: 19980119

A membrane comprising a closely packed array of self-assembling amphiphilic molecules is claimed characterised in that (1) the membrane includes ion channels selected from peptides capable of forming helices and aggregates, podands, coronands, cryptands and combinations and/or (2) at least a proportion of the self-assembling amphiphilic molecules comprise a receptor molecule conjugated with a supporting entity, the receptor molecule having a receptor site and being selected from immunoglobulins, antibodies, antibody fragments, dyes, enzymes and lectins, the supporting entity being selected from a lipid head gp., a hydrocarbon chain, a cross-linkable molecule and a membrane protein, the supporting entity being conjugated with the receptor molecule at an end remote from the receptor site.

Pref. the ion channels are gramicidin or analogues. Also claimed is a biosensor comprising a membrane bilayer attached to a solid surface, the bilayer having an upper and lower layer, the lower layer being adjacent the solid surface and being provided with gps. reactive with the solid surface or with gps. provided on this, each layer of the bilayer being composed of self-assembling amphiphilic molecules and gramicidin monomers, and where a receptor moiety is attached to the gramicidin monomers in the upper layer. The solid surface is pref. a palladium-coated glass electrode.

USE/ADVANTAGE - The membranes are used partic. for the prodn. of biosensors. They have a high density of receptor sites and serve as highly selective binding surfaces to which molecular species to be detected will bind.

Dwq.3/6

L15 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:109884 CAPLUS

DOCUMENT NUMBER: 108:109884

TITLE: Differential localization of glycoconjugates having affinity for concanavalin A on the surface of the

sperm head in the testis, the epididymis, and the

ejaculate of the ram

AUTHOR(S): Delpech, S.; Hamamah, S.; Pisselet, C.; Courot, M.

CORPORATE SOURCE: INRA, Nouzilly, 37380, Fr.

SOURCE: Journal of Experimental Zoology (1988), 245(1), 59-62

CODEN: JEZOAO; ISSN: 0022-104X

DOCUMENT TYPE: Journal LANGUAGE: English

AB The location of Con A receptors on the surface of the head of ram

spermatozoa originating from the rete testis, from 3 regions of the epididymis, or from the ejaculate was investigated by using a Au-Con A labeling technique. Electron microscopic observation revealed 3 major localizations, each being characteristic of the origin of the spermatozoa: periacrosomal in the rete testis, postacrosomal in the epididymis, on the entire surface of the sperm head in the ejaculate.

L15 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

CORPORATE SOURCE:

1987:419734 CAPLUS

DOCUMENT NUMBER:

107:19734

TITLE:

 $\ensuremath{\text{pH-dependent}}$  stability and fusion of liposomes

combining protonatable double-chain amphiphiles with

phosphatidylethanolamine

AUTHOR(S):

Leventis, Rania; Diacovo, Thomas; Silvius, John R. Dep. Biochem., McGill Univ., Montreal, QC, H3G 1Y6,

Can.

SOURCE:

Biochemistry (1987), 26(12), 3267-76

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE:

Journal

LANGUAGE:

English

A series of novel double-chain amphiphiles with protonatable head groups were prepared including acylated derivs. of various 2-substituted palmitic acids, amino acid conjugates of these species, and 1,2-dioleoyl-3-succinylglycerol. These species can be combined with phosphatidylethanolamine (PE) to prepare reverse-phase evaporation vesicles that

are stable and trap hydrophilic solutes at pH 7. At weakly acidic pH values (≤6.5, depending on the titratable amphiphilic component), these pH-sensitive vesicles exhibit fusion, with a limited extent of contents mixing and extensive mixing of lipids, accompanied by leakage of aqueous contents. Protons and divalent cations show strong synergistic effects in promoting mixing of both lipids and aqueous contents between pH-sensitive vesicles prepared with any of a variety of double-chain titratable amphiphiles. Calorimetric results indicate that the relative stabilities of different types of pH-sensitive liposomes at low pH cannot be simply correlated with the propensity of the lipids to form a hexagonal II phase under these conditions. Fluorescence measurements demonstrate that single-chain fatty acids, but not double-chain titratable amphiphiles such as N-acyl-2-aminopalmitic acids, are rapidly removed from pH-sensitive vesicles in the presence of other lipid vesicles, serum albumin, or serum. Addnl., pH-sensitive liposomes containing double-chain titratable amphiphiles retain their aqueous contents better than do those containing single-chain amphiphiles in the presence of lipid membranes or albumin. Surprisingly, however, pH-sensitive vesicles of either type show retention of contents in the presence of serum that is comparable to that observed with vesicles composed purely of phospholipids. A model is proposed to explain these latter findings.

L15 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

1986:84801 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 104:84801

TITLE:

Identifying regions of membrane proteins in

contact with phospholipid head groups: covalent attachment of a new class of aldehyde lipid labels to

cytochrome c oxidase

AUTHOR(S): McMillen, Debra A.; Volwerk, Johannes J.; Ohishi,

Junichi; Erion, Mark; Keana, John F. W.; Jost,

Patricia C.; Griffith, O. Hayes

CORPORATE SOURCE: SOURCE:

Inst. Mol. Biol., Univ. Oregon, Eugene, OR, 97403, USA

Biochemistry (1986), 25(1), 182-93

CODEN: BICHAW; ISSN: 0006-2960

DOCUMENT TYPE:

Journal

LANGUAGE: English

A series of amine-specific reagents based on the benzaldehyde reactive group have been synthesized, characterized, and used to study beef heart cytochrome c oxidase reconstituted in phospholipid bilayers. The series contained 3 classes of reagents, lipid-soluble phosphodiesters having a single hydrocarbon chain, phospholipid analogs, and a water-soluble benzaldehyde. All reagents were either radiolabeled or spin-labeled or both. The Schiff bases formed by these benzaldehydes with amines were reversible until the addition of the reducing agent Na cyanoborohydride, whereas attachment of lipid-derived aliphatic aldehydes was not readily reversible in the absence of the reducing agent. The benzaldehyde group provides a convenient method of controlling and delaying permanent attachment to integral membrane proteins until after the reconstitution steps. This ensures that the lipid analogs are located properly to identify amine groups at the lipid-protein interface rather than reacting indiscriminately with amines of the hydrophilic domains of the protein. The benzaldehyde lipid labels attached to cytochrome c oxidase with high efficiency. Typically, 20% of the amount of lipid label present was covalently attached to the protein, and the number of moles of label incorporated per mol of protein ranged 1-6, depending on the molar ratios of label, lipid, and protein. The efficiency of labeling by the water-soluble benzaldehyde was much less than that observed for any of the lipid

labels because of dilution effects, but equivalent levels of incorporation were achieved by increasing the label concentration ESR spectra of a nitroxide-containing

phospholipid analog covalently attached to reconstituted cytochrome c oxidase exhibited a large motion-restricted component, which is characteristic of spin-labeled lipids in contact with the hydrophobic surfaces of membrane proteins. The line shape and splittings were similar for covalently attached label and label free to diffuse and contact the protein mols. in the bilayer, providing independent evidence that the coupling occurs at the protein-lipid interface. distribution of the benzaldehyde reagents attached to the polypeptide components of cytochrome c oxidase was examined by SDS polyacrylamide gel electrophoresis. The labeling pattern observed for the lipid analogs was not affected by the presence of the nitroxide moiety on the acyl chains but was dependent on the molar ratio of labeling reagent to protein. With the lipid labels, band VII was the most heavily labeled, and significant labeling of bands III, V, and VI was observed at higher labeling ratios. There was little or no labeling of bands I, II, and IV. A different labeling pattern was observed with the water-soluble label, providing addnl. evidence that the lipid-like benzaldehyde reagents react with cytochrome c oxidase from the confines of the bilayer. Thus, these new labels have the necessary specificity and reactivity to be useful in correlating sequence data with the structure and function of integral membrane proteins, particularly in identifying regions in contact with phospholipid head groups at the lamellar interface.

L15 ANSWER 36 OF 38 MEDLINE on STN DUPLICATE 10

ACCESSION NUMBER: 82182979 MEDLINE DOCUMENT NUMBER: PubMed ID: 6176271

TITLE: A novel approach for the topographical localization of

glycolipids on the cell surface.

AUTHOR: Spiegel S; Skutelsky E; Bayer E A; Wilchek M

CONTRACT NUMBER: F32-ES5120 (NIEHS)

SOURCE: Biochimica et biophysica acta, (1982 Apr 23) 687 (1) 27-34.

Journal code: 0217513. ISSN: 0006-3002.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH:

198207

ENTRY DATE:

Entered STN: 19900317

Last Updated on STN: 19970203 Entered Medline: 19820719

AB In this study we have developed a prototype system for distinguishing between the topographical distribution of glycolipids versus glycoproteins on the ultrastructural level. Direct modification of membrane -based sialic acids with biotin groups labels both glycolipids and glycoproteins. In this case, subsequent ultrastructural localization of biotinylated sites would not discern between these two classes of glycoconjugate in an unambiguous manner. When biotinylated cells are fixed prior to interaction with ferritin-conjugated avidin, the mean distance of marker molecules from the membrane bilaver is 8.0 nm. In contrast, if the cells are allowed to cap through the action of ferritin-avidin conjugates on unfixed cells, the average distance (13.0 nm) of the marker molecules appears even more distant from the membrane on the capped portion of the cell (uropod), whereas those on the head region are positioned in close proximity to the bilayer (3.7 nm). In order to exclusively label cell surface glycolipids on the ultrastructural level, bovine brain gangliosides were biotinylated in vitro and the haptenized gangliosides were incorporated into intact cells. In this case, marker molecules denoting the incorporated gangliosides were found in relatively close juxtaposition to the membrane surface, in a manner strikingly similar to the labeling pattern of the head region on capped cells. These results support the concept that, in the native state, the carbohydrate portion of glycolipids is positioned closer to the membrane bilayer than that of glycoproteins.

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         2107 (CAP OR CAPPING) AND MEMBRANE AND ANTIBOD?
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SEARCH ENDED BY USER
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=> py>1999 and 116
         305 PY>1999 AND L16
=> 116 not 117
        1802 L16 NOT L17
=> py>1998 and 118
      63 PY>1998 AND L18
=> 118 not 119
     1739 L18 NOT L19
=> t ti 120 1-50
L20 ANSWER 1 OF 1739
                         MEDLINE on STN
TI Immunolocalization of integrin-like proteins in Arabidopsis and Chara.
L20 ANSWER 2 OF 1739
                        MEDLINE on STN
TI Mechanotransduction molecules in the plant gravisensory response:
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amyloplast/statolith membranes contain a beta 1 integrin-like protein.

- L20 ANSWER 3 OF 1739 MEDLINE on STN
- TI Central root cap cells are depleted of endoplasmic microtubules and actin microfilament bundles: implications for their role as gravity-sensing statocytes.
- L20 ANSWER 4 OF 1739 MEDLINE on STN
- TI Microsomal membrane proteins and vanadate-sensitive ATPase from Vicia faba root tips after clinostat treatment.
- L20 ANSWER 5 OF 1739 MEDLINE on STN
- TI Purification and immunolocalization of an annexin-like protein in pea seedlings.
- L20 ANSWER 6 OF 1739 MEDLINE on STN
- TI Developmental regulation of lymphocyte-specific protein 1 (LSP1) expression in thymus during human T-cell maturation.
- L20 ANSWER 7 OF 1739 MEDLINE on STN
- TI Odontoblast differentiation: a response to environmental calcium?.
- L20 ANSWER 8 OF 1739 MEDLINE on STN
- TI Gamma-glutamyl transpeptidase, an ecto-enzyme regulator of intracellular redox potential, is a component of TM4 signal transduction complexes.
- L20 ANSWER 9 OF 1739 MEDLINE on STN
- TI An analysis of microvessel density, androgen receptor, p53 and HER-2/neu expression and Gleason score in prostate cancer . preliminary results and therapeutic implications.
- L20 ANSWER 10 OF 1739 MEDLINE on STN
- TI Human cementum tumor cells have different features from human osteoblastic cells in vitro.
- L20 ANSWER 11 OF 1739 MEDLINE on STN
- TI The effects of brefeldin A on acrosome formation and protein transport to the acrosome in organ cultures of rat seminiferous tubules.
- L20 ANSWER 12 OF 1739 MEDLINE on STN
- TI A novel dipstick developed for rapid Bet v 1-specific IgE detection: recombinant allergen immobilized via a monoclonal **antibody** to crystalline bacterial cell-surface layers.
- L20 ANSWER 13 OF 1739 MEDLINE on STN
- TI Adducin is an in vivo substrate for protein kinase C: phosphorylation in the MARCKS-related domain inhibits activity in promoting spectrin-actin complexes and occurs in many cells, including dendritic spines of neurons.
- L20 ANSWER 14 OF 1739 MEDLINE on STN
- TI Heterogeneity in the presence of CD4-like molecules on human spermatozoa.
- L20 ANSWER 15 OF 1739 MEDLINE on STN
- TI Virulence and functions of myosin II are inhibited by overexpression of light meromyosin in Entamoeba histolytica.
- L20 ANSWER 16 OF 1739 MEDLINE on STN
- TI Radiation-induced apoptosis in human lymphocytes and lymphoma cells critically relies on the up-regulation of CD95/Fas/APO-1 ligand.
- L20 ANSWER 17 OF 1739 MEDLINE on STN
- TI Peripheral blood lymphocytes from psoriatic patients are hyporesponsive to

- beta-streptococcal superantigens.
- L20 ANSWER 18 OF 1739 MEDLINE on STN
- TI An essential role for the interaction between hyaluronan and hyaluronan binding proteins during joint development.
- L20 ANSWER 19 OF 1739 MEDLINE on STN
- TI The olfactory adenylyl cyclase III is expressed in rat germ cells during spermiogenesis.
- L20 ANSWER 20 OF 1739 MEDLINE on STN
- TI Downregulation of the beta4 integrin subunit in prostatic carcinoma and prostatic intraepithelial neoplasia.
- L20 ANSWER 21 OF 1739 MEDLINE on STN
- TI Molecular cloning and characterization of P47, a novel boar sperm-associated zona pellucida-binding protein homologous to a family of mammalian secretory proteins.
- L20 ANSWER 22 OF 1739 MEDLINE on STN
- TI Association of an 80 kDa protein with C-CAM1 cytoplasmic domain correlates with C-CAM1-mediated growth inhibition.
- L20 ANSWER 23 OF 1739 MEDLINE on STN
- TI Colon carcinoma cells use different mechanisms to escape CD95-mediated apoptosis.
- L20 ANSWER 24 OF 1739 MEDLINE on STN
- TI A crossreactivity at the immunoglobulin E level of the cell wall mannoproteins of Candida albicans with other pathogenic Candida and airborne yeast species.
- L20 ANSWER 25 OF 1739 MEDLINE on STN
- TI Simultaneous quantitation of specific IgE against 20 purified allergens in allergic patients sera by checkerboard immunoblotting (CBIB).
- L20 ANSWER 26 OF 1739 MEDLINE on STN
- Binding of the soluble, truncated form of an Fc receptor (mouse Fc gamma RII) to membrane-bound IgG as measured by total internal reflection fluorescence microscopy.
- L20 ANSWER 27 OF 1739 MEDLINE on STN
- TI Antibody-induced and cytoskeleton-mediated redistribution and shedding of viral glycoproteins, expressed on pseudorables virus-infected cells.
- L20 ANSWER 28 OF 1739 MEDLINE on STN
- TI Superantigenicity of helper T-cell mitogen (SPM-2) isolated from culture supernatants of Streptococcus pyogenes.
- L20 ANSWER 29 OF 1739 MEDLINE on STN
- TI Costimulatory molecules in human atherosclerotic plaques: an indication of antigen specific T lymphocyte activation.
- L20 ANSWER 30 OF 1739 MEDLINE on STN
- TI Epstein-Barr virus-encoded LMP-1 protein upregulates the pNDCF group of nucleoskeleton-cytoskeleton-associated proteins.
- L20 ANSWER 31 OF 1739 MEDLINE on STN
- TI Visualization of Golgi apparatus in methacrylate embedded conifer embryo tissue using the monoclonal antibody JIM 84.

- L20 ANSWER 32 OF 1739 MEDLINE on STN
- TI Leukosialin (CD43, sialophorin) redistribution in uropods of polarized neutrophils is induced by CD43 cross-linking by antibodies, by colchicine or by chemotactic peptides.
- L20 ANSWER 33 OF 1739 MEDLINE on STN
- TI Localization of nerve cells in the developing rat tooth.
- L20 ANSWER 34 OF 1739 MEDLINE on STN
- TI Immunohistochemical localization of nerve fibres during development of embryonic rat molar using peripherin and protein gene product 9.5 antibodies.
- L20 ANSWER 35 OF 1739 MEDLINE on STN
- TI The antigen receptor complex on cord B lymphocytes.
- L20 ANSWER 36 OF 1739 MEDLINE on STN
- TI Identification of two regions in the N-terminal domain of ActA involved in the actin comet tail formation by Listeria monocytogenes.
- L20 ANSWER 37 OF 1739 MEDLINE on STN
- TI Nitric oxide inhibits capping in HL-60 cells.
- L20 ANSWER 38 OF 1739 MEDLINE on STN
- TI Fibrin(ogen) and von Willebrand factor deposition are associated with intimal thickening after balloon angioplasty of the rabbit carotid artery.
- L20 ANSWER 39 OF 1739 MEDLINE on STN
- TI Markers of bone and cementum formation accumulate in tissues regenerated in periodontal defects treated with expanded polytetrafluoroethylene membranes.
- L20 ANSWER 40 OF 1739 MEDLINE on STN
- TI Local accumulation of alpha-spectrin-related protein under plasma membrane during capping and phagocytosis in Acanthamoeba.
- L20 ANSWER 41 OF 1739 MEDLINE on STN
- TI Effects of Ajoene on lymphocyte and macrophage membrane -dependent functions.
- L20 ANSWER 42 OF 1739 MEDLINE on STN
- TI An Aplysia cell adhesion molecule associated with site-directed actin filament assembly in neuronal growth cones.
- L20 ANSWER 43 OF 1739 MEDLINE on STN
- TI Analysis of yeast trimethylguanosine-capped RNAs by midwestern blotting.
- L20 ANSWER 44 OF 1739 MEDLINE on STN
- TI Cell adhesion molecules NgCAM and axonin-1 form heterodimers in the neuronal membrane and cooperate in neurite outgrowth promotion.
- L20 ANSWER 45 OF 1739 MEDLINE on STN-
- TI CD66: role in the regulation of neutrophil effector function.
- L20 ANSWER 46 OF 1739 MEDLINE on STN
- TI Presence of the elastin-laminin receptor on human activated lymphocytes.
- L20 ANSWER 47 OF 1739 MEDLINE on STN
- TI ANCA defines the clinical disease manifestations of vasculitis.
- L20 ANSWER 48 OF 1739 MEDLINE on STN

- TI Association of murine splenocyte CD3 complex to the cytoskeleton: absence of modulation by exogenous fatty acids.
- L20 ANSWER 49 OF 1739 MEDLINE on STN
- TI Association of the tetraspan protein CD9 with integrins on the surface of S-16 Schwann cells.
- L20 ANSWER 50 OF 1739 MEDLINE on STN
- TI Evidence for the presence of immunoglobulin E antibodies specific to the cell wall phosphomannoproteins of Candida albicans in patients with allergies.

=> d ibib abs 120 27,32,44,50

L20 ANSWER 27 OF 1739 MEDLINE ON STN ACCESSION NUMBER: 1998001342 MEDLINE DOCUMENT NUMBER: PubMed ID: 9343177

TITLE: Antibody-induced and cytoskeleton-mediated

redistribution and shedding of viral glycoproteins,

expressed on pseudorabies virus-infected cells.

AUTHOR: Favoreel H W; Nauwynck H J; Van Oostveldt P; Mettenleiter T

C; Pensaert M B

CORPORATE SOURCE: Laboratory of Virology, Faculty of Veterinary Medicine,

University of Ghent, Belgium.

SOURCE: Journal of virology, (1997 Nov) 71 (11) 8254-61.

Journal code: 0113724. ISSN: 0022-538X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199711

ENTRY DATE: Entered STN: 19971224

Last Updated on STN: 19971224 Entered Medline: 19971113

AB Fluorescein isothiocyanate-labeled porcine pseudorabies virus (PrV) polyclonal antibodies were added to PrV-infected swine kidney cells in vitro at 37 degrees C. In approximately 47% of the infected cells, the addition induced passive patching and subsequent energy- and microtubule-dependent capping of all viral envelope glycoproteins, expressed on the plasma membranes of the infected cells. Further contraction and extrusion of the capped viral glycoproteins occurred in approximately 30% of the capped cells 2 h after the addition of antibodies and was accompanied by a concentration of F-actin beneath the caps. At that time, about 18% of the extruded caps were shed spontaneously into the surrounding medium. Mechanical force released 85% of the extruded caps, leaving viable cells with no microscopically detectable levels of viral glycoproteins on their plasma membranes. Experiments with PrV deletion mutants showed that viral glycoproteins gE and gI are important in triggering viral glycoprotein redistribution. Since the PrV gE-gI complex exhibits Fc receptor activity which facilitates capping, the importance of gE and gI may be partially explained by antibody bipolar bridging.

L20 ANSWER 32 OF 1739 MEDLINE on STN ACCESSION NUMBER: 97367997 MEDLINE DOCUMENT NUMBER: PubMed ID: 9224764

TITLE: Leukosialin (CD43, sialophorin) redistribution in uropods

of polarized neutrophils is induced by CD43 cross-linking

by antibodies, by colchicine or by chemotactic

peptides.

AUTHOR: Seveau S; Lopez S; Lesavre P; Guichard J; Cramer E M;

Halbwachs-Mecarelli L

CORPORATE SOURCE: INSERM U90 Hopital Necker, Paris, France.

SOURCE: Journal of cell science, (1997 Jul) 110 ( Pt 13) 1465-75.

Journal code: 0052457. ISSN: 0021-9533.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199709

ENTRY DATE: Entered STN: 19971008

Last Updated on STN: 19971008 Entered Medline: 19970922

AB We investigated a possible association of leukosialin (CD43), the major surface sialoglycoprotein of leukocytes, with neutrophil cytoskeleton. We first analysed the solubility of CD43 in Triton X-100 and observed that CD43 of resting neutrophils was mostly soluble. The small proportion of CD43 molecules, which 'spontaneously' precipitated in Triton, appeared associated with F-actin, as demonstrated by the fact that this insolubility did not occur when cells were incubated with cytochalasin B or when F-actin was depolymerized with DNase I in the Triton precipitate. Cell stimulation with anti-CD43 mAb (MEM59) enhanced this CD43-cytoskeleton association. By immunofluorescence as well as by electron microscopy, we observed a redistribution of CD43 on the neutrophil membrane, initially in patches followed by caps, during anti-CD43 cross-linking at 37 degrees C. This capping did not occur at 4 degrees C and was inhibited by cytochalasin B and by a myosin disrupting drug butanedione monoxime, thus providing evidence that the actomyosin contracile sytem is involved in the capping and further suggesting an association of CD43 with the cytoskeleton. the capped cells exhibited a front-tail polarization with CD43 caps located in the uropod at the rear of the cell. Surprisingly, colchicine and the chemotactic factor fNLPNTL which induce neutrophil polarization associated with cell motility, also resulted in a clustering of CD43 in the uropod, independently of a cross-linking of the molecule by mAbs. An intracellular redistribution of F-actin, mainly at the leading front and of myosin in the tail, was observed during CD43 clustering induced by colchicine and in cells polarized by anti-CD43 mAbs cross-linking. We conclude that neutrophil CD43 interacts with the cytoskeleton, either directly or indirectly, to redistribute in the cell uropod under antibodies stimulation or during cell polarization by colchicine, thus highly suggesting that CD43 may be involved in cell polarization.

L20 ANSWER 44 OF 1739 MEDLINE on STN ACCESSION NUMBER: 97133428 MEDLINE DOCUMENT NUMBER: PubMed ID: 8978825

TITLE: Cell adhesion molecules NgCAM and axonin-1 form

heterodimers in the neuronal membrane and cooperate in neurite outgrowth promotion.

AUTHOR: Buchstaller A; Kunz S; Berger P; Kunz B; Ziegler U; Rader

C; Sonderegger P

CORPORATE SOURCE: Institute of Biochemistry, University of Zurich,

Switzerland.

SOURCE: Journal of cell biology, (1996 Dec) 135 (6 Pt 1) 1593-607.

Journal code: 0375356. ISSN: 0021-9525.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals OTHER SOURCE: GENBANK-Z75013

ENTRY MONTH: 199701

ENTRY DATE: Entered STN: 19970219

Last Updated on STN: 19970219

Entered Medline: 19970117

AB The axonal surface glycoproteins neuronglia cell adhesion molecule (NgCAM) and axonin-1 promote cell-cell adhesion, neurite outgrowth and fasciculation, and are involved in growth cone guidance. A direct binding between NgCAM and axonin-1 has been demonstrated using isolated molecules conjugated to the surface of fluorescent microspheres. By expressing NgCAM and axonin-1 in myeloma cells and performing cell aggregation assays, we found that NgCAM and axonin-1 cannot bind when present on the surface of different cells. In contrast, the cocapping of axonin-1 upon antibody-induced capping of NgCAM on the surface of CV-1 cells coexpressing NgCAM and axonin-1 and the selective chemical cross-linking of the two molecules in low density cultures of dorsal root ganglia neurons indicated a specific and direct binding of axonin-1 and Ng-CAM in the plane of the same membrane. Suppression of the axonin-1 translation by antisense oligonucleotides prevented neurite outgrowth in dissociated dorsal root ganglia neurons cultured on an NgCAM substratum, indicating that neurite outgrowth on NgCAM substratum requires axonin-1. Based on these and previous results, which implicated NgCAM as the neuronal receptor involved in neurite outgrowth on NgCAM substratum, we concluded that neurite outgrowth on an NgCAM substratum depends on two essential interactions of growth cone NgCAM: a trans-interaction with substratum NgCAM and a cis-interaction with axonin-1 residing in the same growth cone membrane.

L20 ANSWER 50 OF 1739 MEDLINE on STN ACCESSION NUMBER: 97071908 MEDLINE DOCUMENT NUMBER: PubMed ID: 8914753

TITLE: Evidence for the presence of immunoglobulin E

antibodies specific to the cell wall

phosphomannoproteins of Candida albicans in patients with

allergies.

AUTHOR: Kanbe T; Morishita M; Ito K; Tomita K; Utsunomiya K;

Ishiguro A

CORPORATE SOURCE: Laboratory of Medical Mycology, Nagoya University School of

Medicine, Japan.. tkanbe@tsuru.med.nagoya.u.ac.jp

SOURCE: Clinical and diagnostic laboratory immunology, (1996 Nov) 3

(6) 645-50.

Journal code: 9421292. ISSN: 1071-412X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199702

ENTRY DATE: Entered STN: 19970305

Last Updated on STN: 19970305 Entered Medline: 19970218

AB To determine the major antigenic component of Candida albicans against immunoglobulin E (IgE) antibodies in the sera of patients with allergies who were positive for IgE antibodies to C. albicans crude antigen in a CAP system, phosphomannoproteins (CAMP/A or CAMP/B for serotype A or B strain, respectively) and their acid-stable portions (CAMP-S/A or CAMP-S/B) were isolated from beta-mercaptoethanol (2-ME) extracts of C. albicans cells of serotypes A and B, and IqE antibodies against these components were compared with those against protein complex and enolase (CAE) fractions isolated from C. albicans cells. The dot blot test, which was used to detect IqE antibodies to the C. albicans antigens, showed that IgE antibodies to the 2-ME extract and phosphomannoprotein fractions were present in the sera of 98.0% (2-ME extract), 96.8% (CAMP/A), 93.2% (CAMP-S/A), 97.2% (CAMP/B), and 81.5% (CAMP-S/B) of the patients, whereas IgE antibodies to the protein complex and CAE fractions were found in the sera of 73.6 and 48.8% of the patients, respectively. The

extent of IgE binding to the 2-ME extract and phosphomannoproteins was well correlated with the fluorescence intensities estimated with the CAP system. Furthermore, the results obtained from the inhibition experiment with the CAP system indicated that the binding of IgE antibodies to Candida antigens is strongly inhibited by the phosphomannoprotein fraction and is an indication that the serum of the patients contained IgE antibodies specific to the cell wall phosphomannoproteins of C. albicans. Finally, an initial chemical analysis indicated that the epitopes for IgE antibodies on the phosphomannoproteins is a carbohydrate portion, since the ability of CAMP/A to inhibit the binding of IgE antibodies to the homologous CAMP/A was destroyed after oxidation by sodium periodate but not after digestion with proteinase K.

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